# Clinical and Pathological

# PAPERS

FROM

# THE LAKESIDE HOSPITAL,

CLEVELAND.

SERIES II.  1905.

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W. T. HOWARD, JR.,
EDWARD F. CUSHING,
HUNTER ROBB,

*Committee on Publication.*

JUNE, 1905.

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## CLINICAL PAPERS.

## PATHOLOGICAL AND EXPERIMENTAL PAPERS.

# CLINICAL PAPERS.

# PARACOLON INFECTIONS, WITH REPORT OF THREE CASES.

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WITHIN the past six years, and especially within the past few months, increasing attention has been drawn to a class of cases which clinically resemble typhoid fever, but which careful bacteriological examination has shown to be due to infection by organisms intermediate between the typhoid and colon bacilli.

For these organisms and the infection which they produce the terms "paratyphoid" and "paracolon" have both been used. Achard and Bensaude,[1] who reported the first cases, entitled them "paratyphoid infections." Widal and Nobecourt[2] opposed this term, and called their organism the paracolon bacillus, claiming that it more closely resembled the colon than the typhoid bacillus. Libman[3] suggests that for the present the term "paracolon" is the preferable one, and would reserve the name "paratyphoid" for those organisms which culturally are identical with the typhoid bacillus, but which are not agglutinated by typhoidal serum.

The earlier reported cases of paracolon infection have been so thoroughly and so recently reviewed that anything more than a brief mention of them seems unnecessary at this time. Achard and Bensaude, in 1896, reported two cases. The first case resembled typhoid fever, and was complicated by double femoral phlebitis and by cystitis or pyelonephritis. From the urine was isolated a paracolon bacillus. The second case was that of an infant which developed suppuration of a sternoclavicular articulation following a febrile attack of some two weeks' duration. The joint was opened, and from the pus was grown a bacillus identical with that obtained from the first case.

In 1897 Widal and Nobecourt isolated a paracolon bacillus from an abscess in the neck, near the oesophagus.

Gwyn,[4] in 1898, reported a case which clinically was typical of typhoid fever complicated by intestinal hemorrhage. From the blood he isolated a paracolon bacillus.

Cushing,[5] in 1900, isolated a paracolon bacillus from a costochondral abscess. His patient had nine months previously suffered from an illness, with relapse, supposed to have been typhoid fever.

In 1900 Schottmüller[6] reported one case, and the following year six additional cases. In all but the last case he isolated paracolon bacilli from the blood; the serum of the seventh case agglutiuated the bacilli from certain of the other patients.

In 1901 Kurth[7] reported five cases which he considered examples of paracolon infection. From the urine of one patient and the feces of another he isolated bacilli which were agglutinated in high dilutions by the serum of four of the cases. The serum of the fifth case—the one with bacilli in the urine—was not tested.

In April of this year Brion and Kayser[8] reported a case of infection resembling typhoid, complicated by relapse and thrombosis of the left leg. A paracolon bacillus was isolated from the blood, urine, feces, vagina, and rose-spots.

In May, 1902, Strong[9] reported an autopsy done forty-two hours after death on a patient who was supposed to have died from typhoid fever. From the spleen was obtained a paracolon bacillus. No lesions were found in the intestinal tract.

In June, 1902, Buxton and Coleman[10] reported a case resembling typhoid fever from whose blood was isolated a paracolon bacillus.

In the same month Berg and Libman[11] reported an interesting case of typhoid fever with a secondary infection with a paracolon bacillus. The clinical picture was that of cholecystitis, and during life the para-colon bacillus was isolated from the gall-bladder, blood, and urine. No typhoid bacilli were cultivated, but the patient's serum agglu-tinated typhoid bacilli at dilutions of 1 : 250, besides giving a reaction with the paracolon bacillus. At autopsy healing ulcers were found in the ileum.

Hume[12] has recently reported a case typical of typhoid fever, with relapse, intestinal hemorrhage, and cystitis. A paracolon bacillus was isolated from the urine and feces.

The last cases, seven in number, are reported in August of this year. Johnston[13] presents four, in two of which paracolon bacilli were isolated from the blood. In the other two the diagnosis was made on the strength of the serum reactions. There were no complications. Hew-lett[14] reports one with isolation of the bacillus from the blood. His patient had a relapse complicated with bronchopneumonia. Longcope[15] reports two cases, with isolation of the bacilli from the blood in both instances. His second case had a relapse. The first case was very severe, and proved fatal on the twelfth day of the disease. At autopsy the intestinal tract was found practically normal. This is the first com-plete autopsy report on a case of pure paracolon infection.

To this list I desire to add the reports of three cases recently observed at Lakeside Hospital. All occurred in the service of Dr. E. F. Cush-ing. The first case is to be reported later from the surgical side. Dr.

G. W. Crile has kindly allowed me to use the surgical records to complete the history.

CASE I. *Paracolon infection; mild course; suppurative cholecystitis during convalescence; incision and drainage of gall-bladder; paracolon bacilli in pus; right lobar pneumonia; recovery.*—M. S., white, male, aged thirty years. Admitted May 13, 1902, complaining of headache, vomiting, loss of appetite, and general weakness. Family and past history unimportant. The present illness began four days before admission, though for two weeks past he had felt weak and drowsy, and had lost his appetite. The initial symptoms were headache, general soreness, slight cough without expectoration, and persistent vomiting. For the past four days he had vomited practically everything taken. Took to bed May 10th.

On examination the patient was well nourished; slightly anæmic. The tongue was dry, coated, and tremulous. Pulse slightly dicrotic. Heart and lungs negative. Liver dulness in the mammillary line extended from the fifth rib to a point two fingers' breadth below the costal margin, where the edge was distinctly felt. The abdomen was

CHART I.
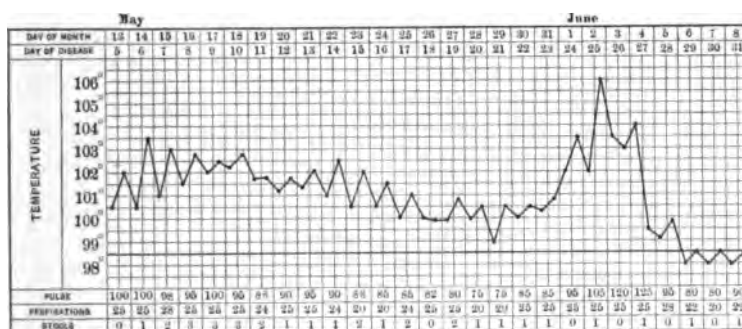


full, tympanitic, not tender. The spleen was readily palpated. There were no visible rose-spots. Temperature. 100.5° F.; pulse, 105; respirations, 25. The urine was high colored, acid, specific gravity 1025; no sugar; trace of albumin; an occasional hyaline cast and a few leucocytes. No diazo reaction.

*May 14th.* Widal reaction negative. No tubercle bacilli in the sputum.

From admission until May 30th the course of the disease was mild and uneventful. The highest temperature was 103.8° F.; it fell slowly and touched normal for the first time on May 29th. On May 18th the patient's serum was tested with a paracolon bacillus, but the result was negative. On May 25th the Widal reaction was again negative. No rose-spots were ever found. The leucocyte count continued normal. In spite of the negative Widal reaction the case was considered to be a mild typhoid.

*29th.* In the evening the patient had an attack of slight abdominal pain associated with nausea and vomiting. Examination of the abdomen was negative, and the pain soon subsided.

*30th.* In the afternoon the patient again complained of abdominal pain, which he described as cramp-like and felt rather generally over the upper right half of the abdomen. The muscles over the right half of the abdomen were held slightly more rigid than over the left, and there was little tenderness on deep pressure in the right half of the umbilical region. Temperature, 100° F.; pulse, 88; respirations, 25. Leucocytes, 12,000.

*31st.* Still slight abdominal pain; nothing additional made out on examination. Lungs and heart negative. Temperature, pulse, and respirations practically unchanged. Leucocytes, 12,000.

*June 1st.* Abdominal pain still complained of, and is now located in the right hypochondrium. There is increased muscular resistance over the right half of the abdomen and decided tenderness in the region of the gall-bladder, which can now be felt as a rounded mass extending to a point 4½ cm. below the costal margin. Temperature at 8 A.M., 102° F.; pulse, 90; respirations, 25. At 8 P.M. temperature, 103.2° F.; pulse, 100; respirations, 28. Leucocytes, 10,000. No bile in the urine; no jaundice.

*2d.* The patient had a comfortable night, and this morning feels much better; abdominal pain almost gone. Examination of the abdomen shows less muscle rigidity and decidedly less tenderness, but the gall-bladder is still palpable and quite sensitive. No jaundice; no bile in the urine. Temperature, 102° F.; pulse, 100; respirations, 25. Leucocytes, 13,000. The question of operation was discussed, but it was decided to await further developments. No change was noticed until 2 P.M., when there was a return of the abdominal pain, and the patient vomited. This was repeated at 3 P.M. At 4 P.M. the patient had a hard, shaking chill, lasting ten minutes, and the temperature rose to 106° F. Aside from increased tenderness over the gall-bladder the abdominal examination remained the same. Leucocytes, 15,800.

Immediate operation was decided upon, and was performed by Dr. G. W. Crile. Cocaine anæsthesia was used. The gall-bladder was found distended and adherent to the parietal peritoneum. On incising it there escaped several ounces of a turbid fluid, which was followed by a small amount of pus. No calculi were found. The gall-bladder was drained and the wound closed. Cultures from the fluid yielded a pure growth of an actively motile bacillus with the characteristics to be described later.

The following day, June 3d, the temperature continued elevated, and the patient complained of cough and expectoration. Examination of the lungs showed a consolidation of the lower right lobe. The next day, June 4th, the temperature fell by crisis, and thereafter continued normal throughout the patient's stay in the hospital. The lung signs cleared up rapidly.

The patient convalesced uninterruptedly, and was discharged July 6th, a very small fistula still remaining at the site of the operation.

CASE II. *Paracolon infection; mild course; cystitis on seventeenth day; thrombosis of left femoral vein on twenty-first day; paracolon bacilli from blood and urine; recovery.*—M. E., male, Australian, aged twenty-six years. Admitted June 6, 1902, complaining of headache, fever, and loss of appetite. Family and past history are unimportant. Present illness began about two weeks ago, with headache, slight cough, and coryza. For a few days had mild diarrhœa; since then has been con-

stipated. Appetite gradually failed, and there has been rapid loss of strength. No nausea or vomiting; no chilliness; no epistaxis. Took to bed the day before admission.

Physical examination showed a well-nourished man looking decidedly ill. Expression dull; face flushed; tongue moist, coated, and tremulous. Pulse of good volume; slightly dicrotic. Lungs negative. Systolic murmur at the apex of the heart; normal area of dulness. Abdomen soft, not tender. Spleen readily palpable. No rose-spots. Liver dulness extended 4 cm. below the costal margin in the mammillary line; edge palpable. Some reddening, swelling, and tenderness about the left ankle-joint, due to a recent injury. Temperature, 105° F.; pulse, 112; respirations, 28. The urine was clear, acid, specific gravity 1019; no sugar; very faint trace of albumin; no diazo reaction; microscopically contained a few coarsely granular casts.

After admission until June 16th the course of the disease was fairly typical of mild typhoid fever. The temperature was slightly irregular, ranging from 100° to 104° F. The pulse was slow, averaging 85 per minute. A few rose-spots were noted, and the spleen was always readily palpable. The leucocytes ranged from 6000 to 9000. The

CHART II.
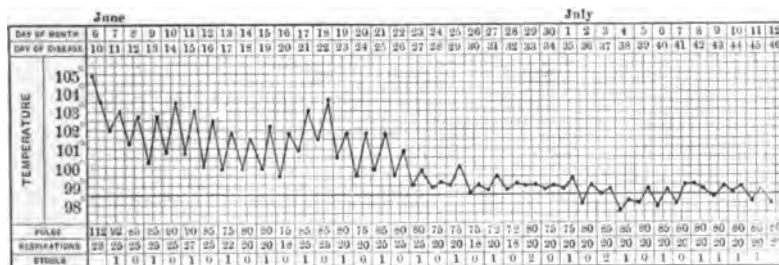


bowels were constipated, requiring enemata. For the first three days it was necessary to catheterize the patient; subsequently he voided urine without difficulty. The Widal reaction, tested frequently, was never positive at dilutions greater than 1 to 10. A blood culture taken June 7th yielded an actively motile bacillus, which will be described below.

On June 16th the patient first noticed slight pain in the left groin, but made no complaint until two days later. Examination at that time disclosed slight swelling of the whole left leg. The foot appeared congested, and there was marked prominence of the superficial veins of the calf and thigh. The surface temperature was not altered. On palpation there was tenderness along the course of the femoral vein and in the popliteal space. The temperature was 103.5° F., which was about 2° higher than it had been running. The leucocyte count was 9000.

Two days later, on June 20th, a definite cord-like thickening could be made out in the upper part of the thigh over the situation of the femoral vein. This was decidedly tender on palpation. Nothing was to be felt in the popliteal space.

On June 13th pus cells were noted in the urine, and on June 21st a culture yielded a large number of colonies of a bacillus identical with that isolated from the blood ; also a few colonies of a streptococcus.

The subsequent course of the disease was uneventful. The temperature reached normal on June 29th, and there was no subsequent rise. The tenderness in the left leg persisted for a few days. The leg never regained its natural size, and the superficial veins remained prominent. Under treatment with urotropin the urine cleared rapidly, and at the time of discharge contained very few pus cells, and no paracolon bacilli could be found on culture. The patient was discharged on July 12th.

CASE III. *Paracolon infection; mild course without complications; recovery.*—D. L., male, white, aged thirty-five years. Admitted June 25, 1902, complaining of fever, loss of appetite, and diarrhœa. Family and past history are unimportant. For the past four weeks patient has

CHART III.
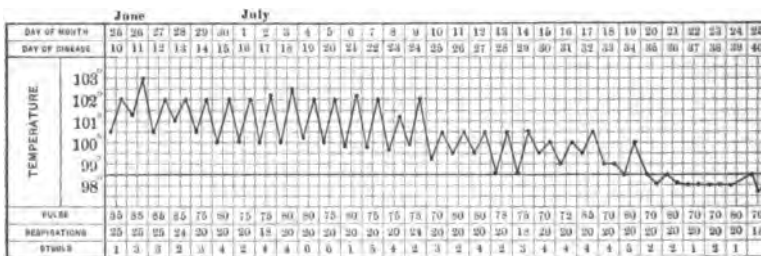


not done any work on account of weakness and loss of appetite. On June 16th had a shaking chill, followed by fever and headache. No subsequent chills ; no epistaxis. The bowels have been loose for a week previous to admission. The patient has remaind in bed since June 16th.

Physical examination disclosed a fairly well-nourished man ; slightly anæmic. Tongue moist, coated, and fissured. Pulse regular, and not dicrotic. Heart and lungs negative. Abdomen held rather rigidly ; no tenderness. Border of spleen palpable ; a few scattered rose-spots ; normal hepatic dulness. Temperature, 100.5° F. ; pulse, 90 ; respirations, 25. Urine clear, acid, specific gravity 1015 ; no sugar or albumin ; microscopically a few leucocytes and an occasional hyaline cast. Diazo reaction positive. Leucocytes, 4400. The Widal reaction, tested on June 29th, July 2d, 11th, and 26th, was persistently negative at dilutions of 1 : 50, though a positive reaction was sometimes obtained at 1 : 10. On July 2d and 11th the patient's serum gave a positive reaction with the organisms obtained from the first two cases at a dilution of 1 : 50.

The course of the disease was that of a mild typhoid fever without complications. The temperature never rose above 103.5° F. It

reached normal July 19th. The bowels were loose throughout the early stage of the illness. Convalescence was rapid and uneventful, and the patient was discharged July 26th. A blood culture on June 29th, the fourteenth day of disease, remained sterile. A urine culture taken during convalescence was negative for paracolon bacilli.

BACTERIOLOGY. The organisms obtained from the first two cases were practically identical, and one description will answer for both. They were very actively motile organisms, having the morphology and staining properties of B. typhosus. The growth on agar and in gelatin was similar to that of B. typhosus. Bouillon was diffusely clouded; no surface pellicle was formed after ten days' incubation. A slight trace of indol was formed in Dunham's peptone medium after one week.

On potato there was a barely perceptible growth appearing as an increase of the moisture along the line of stroke. Litmus milk was slightly acidified after twelve hours; after one week there was distinct reduction of the acidity, and by ten days the color equalled that of the control. After two weeks there was distinct alkali production. The organism from Case I. (" Samuels ") produced slightly more alkali that that from Case II. (" Euster "). There was no coagulation of the milk after four weeks' incubation. Both organisms fermented glucose and maltose, with the production of acid and visible gas, but did not ferment lactose or saccharose. No animal experiments were performed. The organisms agree, therefore, very closely with most of the paracolon bacilli heretofore described.

AGGLUTINATION TESTS. In all the tests a time limit of one hour was used, and a reaction was not called positive unless there was good clumping and cessation of all motility. In none of the cases was a positive Widal reaction obtained in dilutions greater than 1 : 10, though tests were made frequently throughout the course of the disease. The serum from Samuels, Case I., agglutinated B. "Samuels" and B. " Euster " in dilutions of 1 : 100 ; likewise the serum from Euster, Case II., agglutinated B. "Samuels" and B. " Euster " in dilutions of 1 : 200. The serum from Lawton, Case III., agglutinated B. "Samuels" and B. " Euster " in dilutions of 1 : 50. In addition, the sera of Cases I. and II. were tested with Gwyn's paracolon bacillus and one of Johnston's organisms, and in both instances gave positive reactions in dilutions of 1 : 50. B. "Samuels" and B. " Euster " were tested with several different typhoid sera of high agglutinative strength, but without any reaction in dilutions of 1 : 10.

The following table may assist in making these reactions clear:

| Serum. | Organism. | 1–10 | 1–50 | 1–100 | 1–200 |
|---|---|---|---|---|---|
| Samuels. Case I. . . . . | Samuels | + | + | + | — |
| | Euster | + | + | + | — |
| | Gwyn | + | + | 0 | 0 |
| | Johnston | + | + | 0 | 0 |
| | B. typhosus | + | — | — | 0 |
| Euster. Case II. . . . . | Samuels | + | + | + | — |
| | Euster | + | + | + | + |
| | Gwyn | + | + | ? | 0 |
| | Johnston | + | + | + | 0 |
| | B. typhosus | + | — | — | — |
| Lawton. Case III. . . . . | Samuels | + | + | 0 | 0 |
| | Euster | + | + | 0 | 0 |
| | B. typhus | + | — | 0 | 0 |
| Typhoid, agglutinative strength 1–200 . . . . . . . | Samuels | — | — | 0 | 0 |
| | Euster | — | — | 0 | 0 |

0 = no test made.                    ? = doubtful reaction.

Johnston in his recent article has analyzed all the reported instances of paracolon infection. Most of the cases have run a course fairly typical of comparatively mild typhoid fever, and without the aid of the serum reaction or a bacteriological examination a differential diagnosis would be impossible. Rose-spots and a palpable spleen have been present in a majority of instances. Relapse has been comparatively common—at least five cases. Both of Longcope's cases are unusual in that labial herpes was present. The onset of one of his cases was with a chill. Our third case gave a similar history. The very wide distribution of the bacilli in the body is indicated by Brion and Kayser's case.

Many of the common and several of the uncommon complications of typhoid fever have occurred. Of the former there have been reported intestinal hemorrhage, cystitis, femoral phlebitis, furunculosis, and bronchopneumonia; of the latter suppurative arthritis, myositis, osteomyelitis, and suppurative cholecystitis.

Our first case is especially interesting as being the first recorded instance of suppurative cholecystitis complicating a paracolon infection. The clinical picture of Libman's case resembled cholecystitis, but at operation the gall-bladder was distended with dark, thick bile, and at autopsy the bladder wall showed no change. Cholecystitis, both suppurative and non-suppurative, is of course a well-recognized complication of typhoid fever, and its occurrence in a paracolon infection serves to again emphasize the marked similarity of the clinical picture of the two diseases. The ease of performance and the success of early operation in this complication is also well shown in this case.

Longcope in his paper discusses the pathology of the disease. There have been three fatal cases, with autopsies in each instance. Berg

and Libman's case was a mixed infection, probably primarily typhoid fever, with a secondary infection with the paracolon bacillus. Healing ulcers were found in the ileum. In Strong's case no clinical history is available. The autopsy was done forty-two hours after death, and Strong himself suggests that the bacillus isolated from the spleen may possibly have been a post-mortem invader. The large and small intestines were normal throughout. The mesenteric lymph glands were enlarged, and a few were hemorrhagic. Fresh smears from the spleen showed a few crescentic æstivo-autumnal malarial parasites and some pigment; but it seems unlikely that the patient's death was due to malaria. He had been treated with quinine.

Longcope's case is complete. Autopsy revealed only the lesions of an acute infection —acute splenic tumor, cloudy swelling of the liver and kidneys, focal necroses in the liver. The mesenteric lymph glands were not swollen, and both large and small intestine were practically normal.

While no very definite conclusion can be drawn as yet regarding the pathology of the disease, it is evident that we are dealing with an infection quite distinct from typhoid fever. That all of the cases of apparently pure paracolon infection may not, however, be as simple as Longcope's case might lead us to suppose is suggested by the occurrence in two instances of well-marked intestinal hemorrhages.

## REFERENCES.

1. Achard and Bensaude. Bull. et Mém. de la Soc. de Méd. des Hôp., November 27, 1896, p. 820.
2. Widal and Nobecourt. Semaine Médicale, August, 1897, p. 285.
3. Libman. Journal of Medical Research, June, 1902, vol. viii. No. 1.
4. Gwyn. Johns Hopkins Hospital Bulletin, 1898, vol. ix. p. 54.
5. Cushing. Ibid., 1900, vol. xi. p. 156.
6. Schottmüller. Deut. Med. Wochenschr., 1900, vol. xxvi. p. 511; Zeitschr. f. Hygiene, 1901, vol. xxxvi. p. 368.
7. Kurth. Deut. Med. Wochenschr., 1901, vol. xxvii. p. 501.
8. Brion and Kayser. Munch. Med. Wochenschr., April 15, 1902, p. 611.
9. Strong. Johns Hopkins Hospital Bulletin, May, 1902, p. 107.
10. Buxton and Coleman. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1902, p. 976.
11. Berg and Libman. Journal of the American Medical Association, June 7, 1902, p. 1498.
12. Hume. Report of Thompson Yates Laboratories, 1902, vol. iv. p. 385.
13. Johnston. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, August, 1902, vol. cxxiv. p. 187.
14. Hewlett. Ibid., p. 200.
15. Longcope. Ibid., p. 209.

2

# The Character of the Widal Reaction in the Present Epidemic of Typhoid Fever

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Before discussing the Widal reaction of the present epidemic in Cleveland it will be well, perhaps, to give a brief account of the nature of the Widal reaction and of its importance as a diagnostic test in typhoid fever.

In 1894 R. Pfeiffer first discovered that the blood-serum of animals immunized to typhoid fever, when placed in the abdominal cavity of a previously healthy experimental animal, together with an amount of typhoid culture previously determined fatal to an animal of similar size and kind, not only protected that animal against the action of the bacilli but also induced granular degeneration of the bacilli and finally their complete solution.

In 1896, Pfeiffer and Kolle, and independently Gruber and Durham, found that the blood-serum of human beings recently recovered from typhoid fever when mixed with an actively motile culture of typhoid bacilli soon rendered these immobile and caused their clumping together, that is, their agglutination. This was the first time that the reaction was used as a diagnostic measure.

Widal later, in the same year, elaborated the method and showed that the serum of typhoid patients not only exhibited the same agglutinating influence upon the bacillus typhosus after recovery from typhoid fever, but also at the beginning and at the height of the disease.

Numerous workers then took up the study of this phenomenon with the result that the following facts were soon established:

1. That the reaction may occur in 1 to 10 and stronger dilution in health and during the onset of numerous other acute infectious diseases besides typhoid fever.

2. That it is extremely rare when the reaction occurs in dilution of 1 to 20 in other conditions than typhoid fever and that almost never does it occur in dilutions of 1 to 40 or 1 to 50, and above, in other conditions than an existing or past typhoid fever.

3. That the reaction was obtained by Widal and others in dilutions of 1 to 1000 and 1 to 5000, and in one case reported by Widal in which the reaction was positive in dilution of 1 to 20,000.

4. That occasionally, cases clinically typhoid fever fail to give the reaction during their illness, even though in some of these

*Read before the Academy of Medicine of Cleveland, March 18, 1904*

cases the typhoid bacilli can be obtained from the blood during life and in other cases at postmortem.

5. That not for a positive reaction only is agglutination necessary, but also complete cessation of motility in at least 1 to 40 dilution within a time limit of one hour.

6. That competent authorities have obtained the reaction in series of several thousand cases clinically typhoid fever at some time during the course of the disease in from slightly below 90% to 95% of all cases.

7. That in a series of 2500 cases, not typhoid, the reaction was positive in 2% of all cases.

8. That the reaction in mild cases may disappear even before convalescence is established.

9. That the reaction usually persists after convalescence is established from several weeks to several months with instances in which it has persisted 20 and 30 years after the attack.

10. That in order to determine the exact date upon which the reaction becomes positive, frequent examinations during the course of the disease may be necessary.

11. Absence of agglutination during the first or second week of the disease is no evidence against the existence of typhoid fever inasmuch as the reaction may not be positive until the end of the second month.

As regards the day of illness upon which the reaction is positive, Park, in a large series of cases, has furnished the following data:

> Positive in first week 20% of cases.
> Positive in second week 60% of cases.
> Positive in third week 80% of cases.
> Positive in fourth week 90% of cases.
> Positive in two months 75% of cases.

At Lakeside Hospital from January 1, 1903, to March 1, 1904, 454 cases of undoubted typhoid fever were admitted, exclusive of some 60 cases admitted to the Private-Ward Service, and exclusive of quite a number of cases probably typhoid fever, though the physical signs and symptoms were not sufficiently conclusive to warrant my including them in this report in the absence of a positive Widal reaction.

The date of onset of the typhoid fever has in all cases been made from the earliest time when some physical sign or symptom was sufficiently prominent to justify the probable onset of the disease.

I have compiled a statistic report of the total cases admitted during 14 months, and also for each individual month, in order that to show that there has been a definite change in the character of the Widal reaction during the past six months as compared with the preceding eight months.

In performing the reaction the following regulations were observed:

1.  Complete loss of motility and clumping inside of one hour, with a dilution of 1 to 20 and 1 to 50, were necessary before the serum was said to be positive.

2.  Those giving a positive result in dilution of 1 to 20 and a partial reaction 1 to 50 were considered suggestive.

3.  Those never giving a reaction 1 to 20 or 1 to 50 were considered negative.

4.  Cases admitted after the fourteenth day with a positive reaction on admitance were disregarded in compiling this report, as there were no means of knowing when the blood first became positive.

5.  Only those cases which developed positive Widal reaction in the hospital or were admitted with positive Widals before the end of the week were considered.

6.  Upon those admitted with negative Widal reaction the test was performed every third or fifth day during the course of the disease until the reaction was positive, provided it became so at any time.

The following points were determined for each month of the fourteen:

1.  Number of cases.

2.  Earliest date upon which the Widal reaction was positive.

3.  Latest date upon which the Widal reaction was positive.

4.  The average day of illness upon which a positive reaction was obtained.

5.  The number of cases which gave only suggestive reactions.

6.  The number of cases which gave no reaction at any time.

7.  The number of cases which gave a positive reaction 1 to 20 and 1 to 50.

8.  The percentage of cases not positive 1 to 20 and 1 to 50.

9.  The number of cases admitted before the end of the second week.

10.  The number of cases admitted before the end of the second week which gave positive Widal reactions.

11.  The percentage of cases giving a positive Widal reaction before the end of the second week.

12.  The number of cases admitted in the first week.

13.  The number of cases giving positive Widal reactions in the first week.

14.  The percentage of positive Widal reactions in the first week.

15.  The percentage of cases during the last six months which did not give a positive reaction.

16.  The percentage of cases during the preceding eight months which did not give a positive reaction.

17. The percentage of cases during the past six months which gave a suggestive reaction.

18. The percentage of cases during the preceding eight months which gave a suggestive reaction.

19. The percentage of cases during the last six months which never gave any reaction.

20. The percentage of cases during the preceding eight months which never gave any reaction.

### SUMMARY—GENERAL, FOR THE 14 MONTHS

Of these 454 cases 13% did not give positive Widal reactions in dilution of 1 to 50.

10.8% gave suggestive reactions, that is, positive 1 to 20, but not 1 to 50; 2.4% gave absolutely negative results; 86.7% gave positive reactions 1 to 20 and 1 to 50.

The earliest day of illness on which the reaction was obtained was the third, and the latest day of illness on which it was obtained was the fifty-fourth.

Of the 454 cases, 405 were admitted before the end of the second week; 68% gave positive reactions 1 to 20 and 1 to 50 before end of second week. Of the 454 cases, 207 were admitted before the end of the first week; 41% of these gave positive reactions before the end of the first week; 7.5% of the cases admitted during the past six months gave positive reactions before the end of the first week; 46% of the cases admitted in the eight months preceding gave positive reactions in the first week; 58% of the cases admitted in the past six months gave positive reactions before the end of the second week; 71% of the cases admitted during the eight months preceding gave positive reactions before the end of the second week; 15.6% of the cases admitted during the past six months did not give positive reactions 1 to 50; 12.5% of cases admitted in the eight months preceding did not give positive reactions 1 to 50; 11.4% of the cases during the past six months gave suggestive reactions; 10.6% of the cases admitted during the preceding eight months gave suggestive reactions; 4.1% of the cases admitted during the past six months never gave any reaction; 1.9% of the cases admitted during the eight months preceding gave no reaction.

These figures show that the Widal reaction was distinctly delayed in its appearance during the past six months; that it was less often positive in this period of time than was the case previously and that there were more anomalous cases than was the case previously. I wish to thank Dr T. W. Clarke and Dr John Phillips, of Lakeside Hospital, for the aid which they so kindly gave me in making this report.

# COPIOUS WATER-DRINKING AND POLYURIA IN TYPHOID FEVER.

## A CONTRIBUTION TO TREATMENT.

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AND

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DURING the summer months of 1903, when, typhoid fever being unusually prevalent in Cleveland, the wards of the Lakeside Hospital contained many cases of this disease, an attempt was made, at first in the female ward alone, to give much larger quantities, than usual, of water to drink to the fever patients, to determine its effects on their comfort and condition. The free use of water internally is, of course, accepted as important in the treatment of typhoid fever; and it has been the custom in the hospital to see that a patient with this disease should have what was thought an abundant supply. In the nursing directions, three pints daily has been set as the least amount which such a patient should receive; and besides the water given by the nurse, a quart bowlful of ice-water with a bent-glass tube on a stand by the bed-side has enabled the individual to help himself with a minimum of exertion. The twenty-four-hour amount of urine, always measured and charted, has shown in most cases a daily record of from forty to fifty ounces during the time of the fever, and this has been taken as a fair index of sufficient fluid ingestion.

In trying to administer additional water it was soon found, with the efficient help of an admirable head-nurse, that without discomfort or special reluctance on the part of most patients, the unexpected and unusual amounts of from a gallon to a gallon and a half, or even more, could easily be taken. This was accomplished by giving four ounces of water every fifteen minutes during the waking hours, amounting to from eight to fourteen pints, according to circumstances, in the twenty-four hours. In addition the ordinary patient received every two hours during the day, and once or twice at night, alternately six ounces of milk and six ounces

of albumen-water, representing some three pints more of fluid.
These large quantities, so given, were well borne. An occasional
patient rebelled at first at the frequent dosage, but most took
the water readily and some greedily, and the reluctant were, as
a rule, soon persuaded that their comfort was enhanced thereby.
The resulting diuresis was marked. The amount of urine passed in
the twenty-four hours after admission in the average case was found
to be about twenty ounces. After forty-eight hours, or by the end
of the third day, with much uniformity in the abrupt response to
the copious water-drinking, as the charts show, there resulted a
daily elimination of from eight to twelve pints, and even in some
cases two gallons or more of urine; and the polyuria was readily kept
near this level in an uncomplicated case during the febrile part of

CHART I.
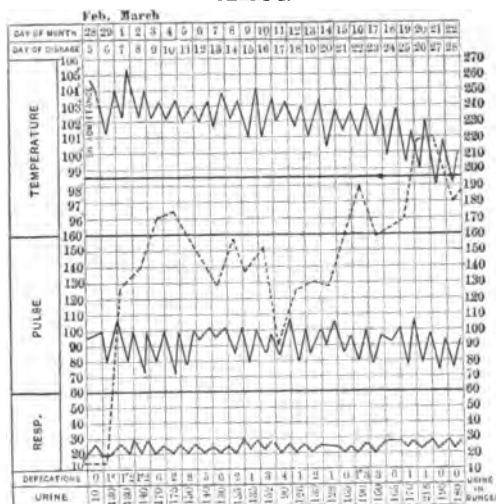


V., Med. No. 4281.   The broken line shows the urine in ounces.

the illness. A daily urine flow of from 120 to 160 ounces was
established and maintained with ease in the average case (Chart I.);
220 ounces and more were not unusual (Charts II. and III.), and in
an occasional instance, like that of Annie M., Medical No. 3720
(Chart IV.), ten ounces were passed on the day of admission, to be
succeeded on the third day by the enormous flow of 431 ounces,
while the average elimination was 270 ounces.

The daily number of typhoid fever cases in the hospital at this
time was from forty to fifty, and the nursing-staff was taxed to
the utmost with the routine care of the patients, and especially
with the great number of tub-baths required. In the ward, however,
where this experiment in hydrotherapy was undertaken, the head-
nurse was soon decided in her judgment that fewer baths were
needed and that the total nursing care of the typhoid patients was

CHART II.



D., Med. No. 4063.    The broken line shows the urine in ounces.    The record was omitted when the temperature became normal.

CHART III.



K., Med. No. 4266.    Abrupt rise in the urine from 10 ounces on the first day to 243 ounces on the second day; maximum, 328 ounces on the ninth day.
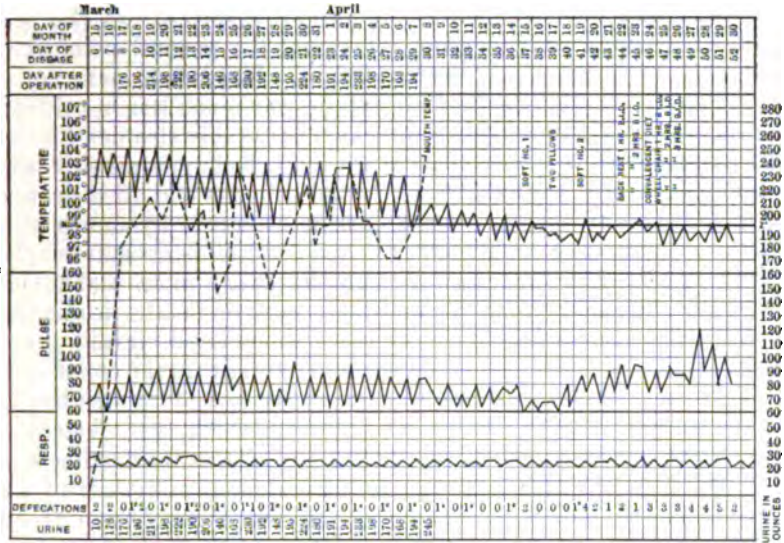
less, in spite of the extra attention which the frequent administration
of water and the increased use of urinals involved.   In the bed-
side observation of this group of cases, the general comfort of
the patients so treated seemed apparent.   Headaches were not so
troublesome, so that the familiar ice-bag was much less in evidence
in the ward.   Tongues and mouths kept noticeably clean and moist,
and the toilet of the mouth cavity was a much simpler nursing task.
Apathy, deafness, restlessness, nocturnal delirium and other nervous
and toxæmic symptoms seemed less in evidence, hypnotics were
not so often needed, nausea was unusual, and remissions in temper-
ature appeared more frequent.   Complications, minor and major,
were few among the patients, and there were no deaths in this first
small series, amounting to twenty cases, though the prevailing epi-
demic was of severe type, and the general mortality in the community
and in the other wards of the hospital at the same time was large.

   An additional year's experience, during which this element of
treatment has been continued with more or less thoroughness in
all the medical wards of the hospital and in the services of Dr.
H. H. Powell, Dr. J. H. Lowman, and Dr. H. S. Upson (I am
greatly indebted to these gentlemen for permission to utilize their
cases), as well as of the writer, has seemed to confirm the early
impression of its usefulness, and demonstrated that in all cases of
typhoid fever, unless on admission profoundly toxic or with serious
complications, or in the case of children who will not, as a rule,
take water so often, this very abundant flow of urine can be secured
with certainty in forty-eight hours and kept up during the illness.
The method of administration first adopted of having the patient
receive, when awake, four ounces of water every quarter of an hour,
has been continued.   Larger quantities at a time are less acceptable,
and often not well tolerated, while small amounts, frequently given,
are usually not unwelcome.

   The urine in these cases when the daily amount exceeds a gallon,
is extremely pale, with a specific gravity of from 1001 to 1005.
With an elimination of more than 200 ounces, the specific gravity
of the watery fluid is often below 1001.   There was found to be a
close approximation in the absence of diarrhœa or sweating, between
the amount of fluid ingested and the quantity of urine eliminated.
Thus in the case of K. (Chart III.), during ten days, 2664 ounces of
fluid were given, while the quantity of urine passed was 2626 ounces,
an average daily difference of some four ounces.   On certain days
the amount of urine passed would slightly exceed the liquid taken.
When obvious perspiration was present, or several loose movements
occurred, the disproportion was, of course, more marked.

   In the case of B., Medical No. 4230, where the skin kept moist
during most of the illness, 1358 ounces of fluid were given in six
days and 844 ounces passed, a daily average of 226 ounces and 140
ounces, respectively.   Chart V. shows the effect of repeated hemor-

CHART IV.
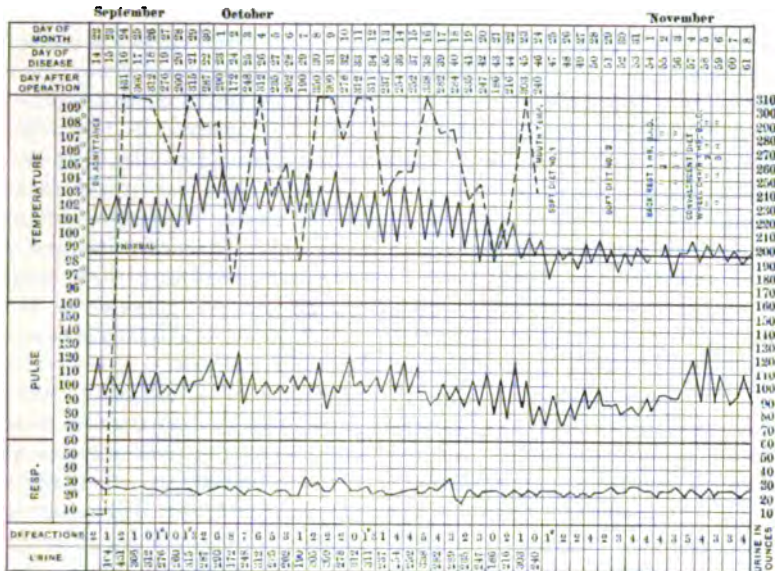


A. M., Hosp. No. 3720.  Extreme case of polyuria, with increase of urine from 10 ounces on the first day to 431 ounces on the second day.

CHART V.



C., Med. No. 4281.  Abrupt rise in urine from 10 to 302 ounces.  The sudden drops in the curve mark the limitation of fluid ingestion following the intestinal hemorrhages.

rhages upon the quantity of urine, with the subsequent stoppage of milk and restriction of water supply.

From June 1, 1903, when the treatment was begun in one of the wards, to October 1, 1904, 100 cases of typhoid fever have shown a daily urine flow of 100 ounces or more; in 56 of this number the amount has been between 100 and 160 ounces; in the other 44 cases, over 160 ounces. During this entire period of sixteen months, 308 cases have been in the hospital, but during the eight months since January 1, 1904, only 105 cases, the improvement in the Cleveland water supply having greatly lessened the frequency of the disease since April, 1904. And as it was not until February, 1904, that this method of water-giving became general in the medical wards, the 100 cases represent a more nearly consecutive series than the discrepancy in totals would indicate.

These cases have been carefully analyzed by Dr. Clarke, who, as resident physician, has had charge of most of them, as to their course, complications, and fatality, and contrasted with a series of 50 cases during the early part of the same period, in which there was no attempt to establish polyuria, and with the 373 cases in the hospital during the year 1903. The duration of *fever* in the two former sets of cases proved precisely the same, 30.7 days; and exactly 8 per cent. of *relapses* occurred in these groups with 11 per cent. in the 1903 series. The average number of tub-baths (given every four hours if the temperature reached 102.5°) in the cases · of urine flow below 100 ounces was 46; of those above 100 ounces, 38.6; of the 44 cases above 160 ounces, 32, pointing to greater remissions of temperature in the polyuria cases. *Bowel movements* were apparently little affected by the large amounts of water ingested, contrary to the expectation that constipation would be less common, and the proportion of cases with regular movements, constipation or diarrhœa was practically the same in the three contrasted series. *Retention of urine* occurred in the first twenty-four hours after admission in 2 cases, and in 1 was persistently troublesome. The thin, watery urine was well tolerated by the bladder, as a rule, and eighteen or twenty ounces were often passed at a time, though with a daily elimination of one or two gallons this involves frequent urination. As much less fluid was given at night, this does not imply disturbance of rest. There were 10 cases of *hemorrhage* in the polyuria group, 8 in the 56 cases below 160 ounces, and 2 in the 44 cases with more than 160 ounces, to compare with 12 per cent. and 6.7 per cent. of the other series. No one of these 10 hemorrhage cases was fatal. One case of *perforation* occurred in the 100 cases; 3 in the group of 50, and 15, the unusual percentage 4 in the 373 cases of 1903. *Phlebitis* was met with but once. The proportion in the other groups being 6 per cent. and 3.5 per cent.; and though the frequency with which venous thrombosis occurs in typhoid varies much, it is conceivable that the copious water-

drinking may lessen the tendency to the formation of agglutination thrombi. *Otitis media* was also infrequent, 3 cases developing, 3 per cent., with 3 in the 50 series, 6 per cent., and 16 in the 1903 series, 4.3 per cent.; and it seems plausible that the clean, moist mouths of these cases may well lessen the likelihood of middle-ear infection. *Meteorism*, however, usually of moderate but in some cases of considerable degree, was more common among the patients taking large quantities of water. Whether a coincidence or in any degree dependent on the treatment does not appear. The *skin* of these patients seemed less dry and harsh than usual; and *furunculosis* occurred only once or twice.

It is regretted that incompleteness of earlier records makes it impossible to compare with accuracy such symptoms as *headache, apathy, restlessness, insomnia,* and mild *delirium;* but the impression is strong in the minds of those who have cared for and watched these patients, whether nurses, house-staff, or the visiting physician, that just these toxic nervous symptoms of the disease, the symptoms so beneficially influenced by the cool-bath treatment of typhoid fever, are still more efficiently controlled by the copious water drinking, employed, of course, as an accessory, not a substitute means of hydrotherapy, and that patients are more comfortable for the treatment.

The total *mortality* of the polyuria group of 100 cases was five, 5 per cent. Four deaths occurred among the 54 cases with an elimination below 160 ounces, 1 death in the group of 46 cases where 160 ounces were exceeded. The latter case, after a severe illness, but when apparently convalescing satisfactorily, died on the sixth day of normal evening temperature, with an acute dilatation of the right heart. The other four fatalities were due, one to toxæmia one to perforation, one to laryngeal perichondritis, and one to peritonitis following an operation for suspected perforation. The mortality of the 308 cases in the hospital during the period under consideration from June, 1903, to October, 1904, and including the 100 polyuria cases, was 7.8 per cent., with twenty-four deaths. The mortality of the year 1903 was, however, usually large, 10.2 per cent. of a total of 373 cases, and the last half of this year with its large quota of patients not having such quantities of water internally, contributes two-thirds to the entire group of 308 cases. The death rate of the 105 patients discharged from the hospital during the eight months from January 1 to October 1, 1904, has been 6.6 per cent.

From March 1st to October 1st, the period during which all patients, with few exceptions, have received this form of treatment, there have been 77 cases with 3 deaths, 3.9 per cent, and, to date (October 11th) 86 cases with a mortality of 3.4 per cent. Finally, from April 1, 1904, to October 11, 1904, the rather unusual consecutive series of 56 cases without a death has occurred.

| | Below 100 ounces. 50 cases. | Above 100 ounces. (Polyuria series.) 100 to 160 ounces. 56 cases. | Over 160 ounces. 44 cases. | Total 100 cases. | All cases. 1903. 878 cases. |
|---|---|---|---|---|---|
| Days of fever. | 30.7 | 31.6 | 29.6 | 30.7 | ...... |
| Highest temperature. | 104.5 | 104.4 | 104.2 | 104.3 | ...... |
| Number of baths. | 46 | 44 | 32 | 38.6 | ...... |
| **Condition of bowels** — Constipation. Per cent. | 38 | 43 | 53 | 46 | ... |
| Constipation. No. | 19 | 23 | 23 | 46 | ... |
| Regular. Per cent. | 46 | 36 | 34 | 35 | ... |
| Regular. No. | 23 | 20 | 15 | 35 | ... |
| Diarrhœa. Per cent. | 8 | 18 | 9 | 14 | ... |
| Diarrhœa. No. | 4 | 10 | 4 | 14 | ... |
| **Complications** — Relapse. Per cent. | 8 | 9 | 7 | 8 | 11 |
| Relapse. No. | 4 | 5 | 3 | 8 | 40 |
| Hemorrhage. Per cent. | 12 | 14 | 4 | 10 | 6.7 |
| Hemorrhage. No. | 6 | 8 | 2 | 10 | 25 |
| Perforation. Per cent. | 6 | 2 | 0 | 1 | 4 |
| Perforation. No. | 3 | 1 | 0 | 1 | 15 |
| Otitis media. Per cent. | 6 | 4 | 2 | 3 | 4.3 |
| Otitis media. No. | 3 | 2 | 1 | 3 | 16 |
| Phlebitis. Per cent. | 6 | 0 | 2 | 2 | 3.5 |
| Phlebitis. No. | 3 | 0 | 1 | 1 | 13 |
| Meteorism. Per cent. | 14 | 25 | 39 | 31 | ... |
| Meteorism. No. | 7 | 14 | 17 | 31 | ... |
| **Mortality** — Total mortality. Per cent. | 12 | 7.2 | 2 | 5 | 10.2 |
| Total mortality. No. | 6 | 4 | 1 | 5 | 38 |
| Toxæmia. Per cent. | 2 | 2 | 0 | 1 | 3.5 |
| Toxæmia. No. | 1 | 1 | 0 | 1 | 13 |
| Pneumonia. Per cent. | 4 | 0 | 0 | 0 | 1.3 |
| Pneumonia. No. | 2 | 0 | 0 | 0 | 5 |
| Perforation. Per cent. | 6 | 2 | 0 | 1 | 3.7 |
| Perforation. No. | 3 | 1 | 0 | 1 | 14 |
| Rare causes. Per cent. | 0 | 4 | 2 | 3 | 1.6 |
| Rare causes. No. | 0 | 2 | 1 | 3 | 6 |

As the 100 cases of typhoid fever with polyuria reported represent, in some measure, a selected group, the small and diminishing mortality rate is, of course, at the most, suggestive. It is felt, however, that certain conclusions as to the results and usefulness of this mode of treatment, which seems to supply an additional means of combating the toxæmia of the disease, may be submitted with some confidence with the hope that this method of copious water–drinking with its resulting diuresis, may be found by other observers to diminish in some further degree the severity and mortality of typhoid fever in hospital practice.

Our experience and conclusions may be summarized as follows:

1. Large quantities of water internally, a gallon or more in twenty-four hours, may easily be taken by typhoid fever patients, if administered in small quantities at frequent and definite intervals.

2. A copious elimination of watery urine at once follows, the degree of polyuria, day by day, closely corresponding to the quantity of fluid ingested.

. 3. Patients are more comfortable by this mode of treatment and toxic, nervous symptoms are lessened.

4. The mortality, as well as the severity, of typhoid fever, seems to be still further diminished by this method of hydrotherapy employed as an accessory to the cool-bath treatment of the disease.

# STOMATITIS IN IMPETIGO CONTAGIOSA.*

## BY EDWARD F. CUSHING, M.D.,

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The occurrence of a form of stomatitis in impetigo contagiosa has been specially referred to in French pediatric and dermatological literature. Comby[1] called attention to this association seventeen years ago, and has several times returned to the topic, describing *"stomatite impétigineuse"* as a characteristic and not infrequent complication of acute facial impetigo.

Bergeron[2] in France, Bohn[3] in Germany, and J. F. Payne,[4] of St. Thomas' Hospital, in England, had previously reported instances of ulceration of the lips and mouth in children with impetigo contagiosa. Payne in his cases noted, also, the occasional inoculation of the disease on other orificial mucous membranes with a resulting purulent coryza, conjunctivitis, keratitis, or vulvovaginitis; and from the quite frequent combination of stomatitis and the whitlow-like lesions on the fingers used "hand and mouth disease" as a synonym of his own for the affection. He has again discussed the subject in his recent article[5] in Allbutt's System. To Bergeron and Comby, however, seem due the detailed clinical picture of this variety of stomatitis.

The lesions of impetiginous stomatitis bear a certain resemblance to those of herpetic or aphthous stomatitis. Their usual seat is on the inner surface of the lower lip, but they may occur on the inner surface of the cheeks, or of the upper lip, on the tip of the tongue, or on the gums, but always in the front of the mouth where the child's fingers might have reached. A pustular or crusted skin patch on the outer border of the lip may be directly connected with an ulceration on the mucous membrane within. The mouth lesions are single or few in number, not grouped like herpetic ulcerations, larger, as a rule, than the latter, irregular in outline, presenting themselves as slightly raised patches of a pearly-gray appearance when recent, and later of a grayish-white

* Read before the Ohio State Pediatric Society, Cleveland, O., May 16, 1904.

or yellowish hue. The patches are quite adherent, and their re-
moval exposes a raw and bleeding surface. The surrounding
mucous membrane is more or less reddened, and there may be in-
crease of saliva, but no odor to the breath, and little or no local
discomfort. The lymph nodes under the chin are slightly swollen
and tender. The process remains superficial, and healing occurs,
as a rule, within a fortnight. The diagnosis is simplified by the
presence of a skin eruption of impetigo, though Comby has seen
the lesions in the mouth precede those on the skin. He also, de-
scribes involvement of other mucous membranes with purulent
rhinitis, conjunctivitis, and vulvovaginitis, and explains all the
lesions, as well as the common paronychia, as the result of auto-
inoculation from scratching or rubbing and the introduction of the
finger into mouth, nose, or elsewhere.

Sevestre and Gaston,[6] Dupuy,[7] Leroux,[8] Poulain,[9] Levy[10] and
others in France, have studied impetiginous stomatitis as well as
the other secondary lesions of the nose, eyes and vulva, clinically
and bacteriologically. All regard these complications, when
looked for, as not infrequent. Bacteriological examination shows
in all cases *staphylococcus aureus,* as in the skin pustules of
impetigo. Leroux and Balzer and Griffon,[11] however, have
isolated a streptococcus from early lesions on both the skin and
mucous membranes, which by inoculations has produced char-
acteristic lesions on the skin, furnishing anew the same organism,
and they regard the staphylococcus as a secondary invader.

In recent German literature, also, there is a recognition of the
occasional involvement of the mucous membranes in impetigo
contagiosa. Lang,[12] of Vienna, in his text book, of 1902, describes
these complications; and Mikulicz and Kümmel[13] in their ex-
haustive work on diseases of the mouth, refer to the subject.
Jadassohn[14] in 1896 reported the successful inoculation of im-
petigo lesions on the skin from the mouth patches of the disease.

Excepting Payne's papers, however, I know of no discussion
of the subject in English or American dermatological or pediatric
text-books or journal literature. Forchheimer[15] in his admirable
monograph on the diseases of the mouth in children, in 1892,
alludes to the topic in the single sentence that "the fact that
aphthæ may be found in the mouths of children with impetigo is
of no possible value in establishing any connection between them."
H. G. Anthony,[16] of Chicago, in 1898, reporting 50 cases of im-
petigo contagiosa notes of one what may serve as a very good

description of impetiginous stomatitis, as follows:—"A child of three had the ordinary form on the chin, together with lesions on the mucous membranes of the mouth, which were not aphthous, but greatly resembled syphilitic mucous patches; they had appeared shortly after the chin lesions. There were no syphilitic lesions on other parts of the child's body and no history of syphilis in the child or its parents. Scrapings from these lesions contained staphylococci, but no oidium albicans. They healed promptly under treatment by peroxid of hydrogen."

It is obvious that the possible involvement of the mouth, the mucous membrane of the nose, the conjunctiva, or the vulva in impetigo contagiosa present problems of differential diagnosis of interest to the pediatric physician. In so common a disease, where a glance usually suffices for diagnosis, and in the uncleanly type of children, commonly affected and seen in dispensary clinics, it is easy to appreciate that a running nose, inflamed eyes or sore mouth may be overlooked, or not suspected to represent an integral part of the disease.

These complications of impetigo contagiosa were brought to the writer's attention by the following cases:—

CASE I.—*Impetiginous Stomatitis.* Charles P., six years old, was admitted to the Children's Ward of the Lakeside Hospital, under suspicion of typhoid fever. For a few days he had been listless, complained of headache and seemed feverish at night; the bowels had been constipated and he had vomited once. The boy was well-nourished and of good color, but was apathetic. Temperature 99.5° F., pulse 100. Examination was negative, except for lesions of impetigo on the face. In the middle of the forehead, on the upper lip at the orifice of the left nostril, and on the chin, were typical crusts of impetigo contagiosa, those on lip and chin brownish-red from blood admixture. There was slight mucopurulent discharge from the left nostril. The tongue was coated, the mouth and throat otherwise negative. The submaxillary and submental lymph nodes were slightly enlarged. There was no Widal reaction, and the leukocyte count was 11,000. The urine was normal. The child continued apathetic and drowsy for three or four days, the temperature ranging from 99° to 100° F. On the fifth day the temperature was normal, and the boy bright and hungry. The facial lesions were tending to heal. On the next day there was found on the inner surface of the lower lip near the right angle of the mouth a pearly-white, irregularly rounded

lesion, ¼ inch in diameter, slightly raised above the mucous membrane, closely adherent, without red areola, but presenting a superficial resemblance to a lesion of herpetic stomatitis. The next day, a slightly larger patch of the same appearance was noted on the inner surface of the right cheek opposite the first molar. There was general redness of the mouth and some increase of saliva. The lymph nodes under the chin on the right side showed increased enlargement and tenderness. The thin, smooth, gray-ish-white patches, dull and opaque in look, did not resemble a diphtheritic membrane and were not pultaceous. The surface layer was closely adherent and left a raw, red surface on removal. There were no further lesions, and in the course of eight days, the patches gradually cleared. Meanwhile, the facial lesions had healed. Cultures from the under surface of one of the mouth lesions gave a pure culture of staphylococcus aureus.

CASE II.—*Impetiginous Rhinitis.* Mabel B., six years old, was brought to me because of a profuse purulent discharge from the left nostril of some days' duration. The character of the discharge suggested an inflammation of one of the sinuses, or the presence of a foreign body in the nostril. Examination, except for redness and swelling of the tissues, was negative. An older sister with whom the child slept, had been seen a few days before, with facial impetigo. No suspicion of the bearings of this fact on the purulent rhinitis was excited, until a typical pustule of impetigo appeared on the upper lip of the patient. Bacteriological examination of the nasal discharge showed staphylococcus aureus in pure culture. With simple treatment, the purulent secretion from the nostril subsided as the facial lesion healed.

## BIBLIOGRAPHY.

1. Comby. La France méd. 24 Dec., 1887.
   De quelques stomatites de l'Enfance. Rev. mens. d. Mal. de l'Enfance. Sept., 1888, p. 916.
   Soc. méd. des hôp. d. Paris, 1891, p. 330. (Discussion of Sevestre's communication.)
   Traité des mal. de l'Enfance. (Grancher-Comby-Marfan) Stomatite impétigineuse. 1897. Vol. VII., p. 362.
2. Bergeron. Stomatites. Diet. encyclopéd. d. sci. méd. (Dechambre.) 1880.
3. Bohn. Die Mundkrankheiten. Gerhardt's Handbuch d. Kinderkrank. Vol. IV., p. 2, 1880.

4. Payne, J. F. St. Thomas' Hosp. Rep., Vol. XIII., p. 301, 1883.

5. Payne. Impetigo Contagiosa. Allbutt's System. Vol. IX., p. 526.

6. Sevestre et Gaston. Sur une variété de stomatite diphtéroide à staphylocoques. Soc. méd. d. hôp. d. Paris, 26 June, 1871, p. 316.

7. Dupuy. Sur l'impetigo et certaines de ses localisations chez l'enfant. Thèse de Paris, 1891.

8. Leroux. De l'impetigo des enfants, affection contagieuse, inocuable, et microbienne. J. d. clin. et. d. thér. enfant. 8 March, 1894, p. 210.

9. Poulain. Thèse de Paris. 2 March, 1892.

10. Levy. Thèse de Nancy, 1897.

11. Balzer et Griffon. Le streptocoque, agent pathogène constant de l'impetigo. C. R. Soc. d. Biologie, 29 Oct., 1897, p. 916.
    Stomatite diphtéroide impetig. à streptocoque. Rev. mens. d. mal. de l'Enfance. Jan., 1898, p. 23.

12. Lang. Lehrbuch d. Hautkrankheiten, 1902, p. 224.

13. Mikulicz. u. Kümmel. Die Krankheiten des Mundes. Jena. 1898, p. 233.

14. Jadassohn. 73 Jahresber d. schles. Ges. f. vaterl. Kultur. Med. Sektion, 1896, p. 89.

15. Forchheimer. Diseases of the Mouth in Children, 1892, p. 38.

16. Anthony, H. G. J. Cutan. and Genito-urin. Dis., 1898, Vol. XVI., p. 227.

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# A REPORT OF TWO CASES OF "TYPHOID SPINE."[1]

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SINCE 1889 several examples of a rare sequel or complication of typhoid fever have been reported under different names. That of "typhoid spine" is the one first used and possesses the advantage of not binding one to a definite theory of the underlying pathological cause. I have succeeded in finding references in the literature to twenty-one cases having some resemblance or relation to the condition first reported under this name, and to these I take pleasure in adding the histories of two others which came under my care at the Lakeside Hospital during my service as resident physician.

CASE I. J. F. C., male, age twenty-eight years, agent structural steel work; entered the Lakeside Hospital on the eighth day of his illness with typhoid fever. The attack, while not marked by extremely high temperature, was a severe one complicated by intestinal hemorrhage, relapse and furunculosis. The Widal and diazo reactions were obtained. Although there were no symptoms referable to the back during his stay in bed, it was noticed later that it was exceptionally weak and ached after the patient was allowed to sit up or walk about. There was no actual pain. The back was examined several times with entirely negative results.

[1] Read before the Academy of Medicine of Cleveland, June 20, 1902.

The patient left on the 6th of June, 1899, after a stay of seventy days in the hospital. On the 23d of August he re-entered the hospital, complaining of pain and weakness in the lower lumbar region, and gave us the following account of his illness: For ten days after his discharge his back was weak and ached a little; then without assignable cause he began to have pain which was slight at first but increased rapidly in severity. At the beginning it was throbbing in character but later became dull. This dull pain began to be punctuated by sudden short attacks of severe pain; the sharp pains were associated with a great tendency to twitch, and any movement intensified and prolonged the attacks. The pains were somewhat more severe when the patient drew up his legs, and were a little relieved if the legs were in a horizontal position or nearly so. The duration of these attacks was usually an hour or two, with intervals of from three to four hours of comparative relief. Movement caused pain, and was very apt to bring on an attack of this kind, which, however, often began without assignable cause. The attacks were more frequent at night than in the day time, and disturbed his sleep. The localization of the pain was in the lower lumbar and sacral region or buttock; most commonly on the right side, sometimes on the left, never on both. Previous to his admission to the hospital the patient states that opiates were discontinued, because on trial they were found to have so deleterious an effect on the action of the kidneys and bowels. During the severest part of the illness the patient had periods of a few days each with normal temperature, alternating with febrile periods of similar duration in which the temperature sometimes rose to 108° F. At this time he became much emaciated and nervous, "going all to pieces" if he lost control of himself. His bowels were constipated. About four weeks before his readmission to the hospital he began to

improve. The attacks of pain became less fre-
quent and severe, the appetite improved and he
gained in weight.

At entrance the appetite was good, the bowels
were regular, and the pain was confined to the
lower lumbar region, was dull in character, with
an occasional sharp twinge. The physical exam-
ination was largely negative. The patient was
somewhat emaciated; the pulse 80, regular and
rhythmic; the patellar reflexes were very weak,
the plantar reflex was not obtained. There was
no evidence of destructive disease of the spinal
column; no deformity; no tenderness over the
spine or elsewhere; no indication of involvement
of the sciatic or other great nerve trunk; no evi-
dence of psoas abscess. The urine is reported
not to have contained albumin; there was no
diazo reaction; the sediment showed a few hya-
line and fine granular casts and leucocytes.
Examination of the blood revealed the presence
of 5,280 leucocytes to the cubic millimetre. The
Widal reaction was reported negative.

During the first month of his second stay in the
hospital the patient was not kept continuously in
bed, and was at times almost free from discom-
fort, and again suffered considerable pain in his
back or in his buttock. At the end of his first
month in the hospital the temperature, which had
varied between 98° F. and 99° or 99.5° F., began
to go up gradually, reaching its highest point,
103.6° F., on the 25th of September. The febrile
period extended over two weeks. Shortly after
this rise in temperature began, an examination of
the blood showed 8,800 leucocytes to the cubic
millimetre. On the 2d of October the spleen,
which is said to have been normal in size at en-
trance, was felt below the costal margin, and a
Widal reaction was obtained. There was no rose-
rash, the abdomen was neither distended nor tym-
panitic. In spite of the enlargement of the spleen
and the apparent recurrence of the Widal reac-

tion, it is hard to see how this could be either a reinfection with typhoid or a relapse of that disease. At first it was not thought necessary to confine the patient strictly to his bed. The Paquelin cautery was used on several occasions, the back was strapped, and tonic remedies were employed. When the more severe pain began, antirheumatic, antineuralgic, sedative and hypnotic remedies were employed, with opiates when necessary. The case progressed without the aid of any mechanical contrivances aside from the very inadequate one of adhesive straps. When the patient was in bed with severe pain, with a view to determine whether relief would be afforded by the use of extension by weight and pulley, manual extension was tried without any apparent benefit. Until perhaps the last of October there was very little change in the condition of the patient as to pain, but from that time on there seemed to be a steady, but very slow improvement in this respect. On the 2d of November he began to have a bed-rest very cautiously, and this was gradually increased, as the procedure seemed to be tolerated and the patient's strength bore it. He was discharged from the hospital on the 13th of December, 1899, the note stating that he had still some trouble with his back.

The patient was seen in July, 1901, and said that, except for two to three days about three weeks after leaving the hospital, he had no pain or ache in the back after his discharge, but that he had so much weakness in the back that he greatly feared a return of the trouble on several occasions. He did not attempt to go to work in the office until May, 1900, thirteen months from the onset of the typhoid, and, for some time after returning to the office, did very little. During all the next summer had a good deal of soreness in the back for a day or two after any misstep or overexertion, and experienced considerable difficulty in getting about on this account. At the

present time he does about the same as he did be-
fore his sickness, but still has a little soreness in
the back after a misstep or overexertion. He is
quite certain, however, that this last is decreasing
and will entirely disappear.

CASE II. J. M. H., male, age forty-two years,
a salesman in a large hardware store, entered the
Lakeside Hospital July 17, 1899, in the service of
Dr. J. E. Cook, by whose kind permission I am
permitted to report the case. Unfortunately the
records of the case were not preserved, but the
following history has recently been secured from
the patient, a very intelligent man, and I think
that the general features of the attack have not
been in any way misrepresented by the loss of
the original records. To Dr. Cook I am indebted
for certain facts about the case not remembered
by the patient or myself. He was taken ill with
typhoid on the 7th of April, 1899. About seven
weeks later the fever left, the course being one of
only moderate severity and entirely without com-
plications in the preliminary attack. At about
the usual time after the disappearance of the
fever, the patient was propped up in bed, and
felt a little stitch or catch in his back such as one
has at times on twisting it. This trouble increased
continuously, and within twenty-four hours he
was unable to turn in bed, and suffered from
deep, cramp-like pain in the lower lumbar region,
a little more to the right than to the left. This
pain was not absolutely continuous, but came in
paroxysms, which seemed to be relieved, or at least
to be made more bearable, if the patient grasped
the bed or some other object tightly while it
persisted. After this first bed-rest and its very
unpleasant sequel, he was kept flat upon his back
fully ten days, and at the end of that time was so
much relieved that he was again propped up in
bed. The time of the bed-rest was very gradually
increased, and he was allowed to put on his
clothes at the end of another ten days. He was

not, however, free from pain or soreness when sitting up, but when lying down he had no discomfort. There was no elevation of temperature. At the end of about two weeks the pains again began to increase, and one day when on his feet he had so severe a "cramp" that he would have fallen if it had not been for support. He thereupon took to his bed and for three or four days had some elevation of temperature.

On the 17th of July he entered the hospital. The patient was anemic, emaciated and nervous, being almost hysterical at times. There was no evidence on physical examination of a neuritis ; no deformity of the spine was detected ; no tenderness to deep pressure was found in either iliac region or over the painful area in the back. Tenderness over the spine developed later and was for a time very marked. There were no rectal or vesical symptoms. Fortunately I have been able to find the original record of his temperature for the first thirty-eight days of his stay in the hospital. He entered with a normal temperature, but during the first month he had febrile periods of from twelve hours to four days in duration, in which the temperature rose to 102.5° F., 103.5° F., and once to 104.7° F. They alternated with rather longer periods of normal temperature. After the first month in the hospital his temperature is supposed to have remained normal. The patient was never free from discomfort at entrance, and at relatively short intervals would have a succession of spasms of pain lasting at intervals for a day and a night, or even two days, after which he would be relatively free from them for a short time. Absolutely no cause could be assigned for the onset of these attacks, although any movement except one executed with the greatest circumspection increased his discomfort, whether he was in pain or relatively free from it at the time. For about one week from the time of entrance heat was applied to his back. During the second

week cold was applied by means of an ice bag.
Morphia was used throughout when it was con-
sidered necessary. Dr. J. H. Lowman saw the
case in consultation during one of the attacks of
pain, and suggested the use of extension by means
of a weight and pulley, on finding that manual
extension afforded relief. Extension was applied,
and was continued intermittently for about four
weeks. In spite of the fact that it afforded an
appreciable amount of relief, it was not continued
more than a few hours each day, since its appli-
cation disturbed the patient, and it was thought
desirable to allow him to turn on his side with
the hope of thus avoiding bed sores. In addition
to tonic remedies, potassium iodode was admin-
istered in moderate doses, and opiates were used
as needed for the relief of pain. For a consider-
able time after entrance the prognosis was con-
sidered very grave. He was thought to have a
tuberculous spondylitis. From the time of the
first bed-rest till the patient was discharged from
the hospital, "improved," advances were made
very gradually. He had his clothes on for the
first time about three weeks before he went home.

The patient was seen in July, 1901, and stated
that he returned to the store in January, 1900,
but did very little work for eight or nine months,
and had an aching, weak back all the time. Any
jar or misstep or stubbing the toe would hurt his
back. It was well on in the spring of 1901 be-
fore he could lift anything at all heavy, and when
seen was unable to scuffle, and felt a hurt in the
back at times when "doubling up," especially
before a storm. He would hesitate to lift weights
greater than one hundred pounds, which was the
most he was called upon to attempt, but within
these limits he did anything that came his way in
the hardware business. He had considered him-
self well for the few months preceding the time
he was seen in 1901.

The case reported by Eskridge[4] is quite in-
accessible, and the history is of such interest that
it seems desirable to give an extended abstract
in this place. E. S., male, Germany, hostler.
Mother died of brain fever in the thirty-fifth
year. Maternal grandfather died of hemiplegia.
Family history otherwise unimportant. The pa-
tient had been a hostler for the preceding six
years. For the preceding eight or nine years
he had joint pains in damp weather. Five years
ago he contracted syphilis. Four years ago he
was lame for two months from pain in the sacral
region, and the pain extended to the left side of
the pelvis. Two years before the present attack
he moved from his former home in Illinois to
Denver. Since his stay in Colorado his joint
pains seem largely to have disappeared. In July,
1892, he was admitted to the Arapahoe County
Hospital suffering from an attack of typhoid
fever. During his convalescence he began to
complain of pain in the sacral region. At first
it was simply stiffness after sitting, with some
pain when he attempted to get up. This passed
off after he walked about for a short time. About
the middle of September he left the hospital and
returned to work, but the pain in the back and
the parts around the left hip became so great that
he was compelled to give up work and return to
the hospital. After his return to the hospital he
was confined to bed on account of pain. When
the patient stood both legs were straight and the
gluteal folds were normal. The legs could both
be abducted and adducted without pain. Ex-
tremes of flexion and extension of the left thigh
caused great pain. The back was painful on
pressure over the first sacral spine, and the
tenderness was limited to one spinous process.
Pressure here caused pain to shoot down the
posterior portion of the left thigh, and in the
region of the small sciatic nerve on the same
side. When the left leg was straightened and

brought forward, it gave rise to pain in the sacral region of the spine, in the left hip, and in the posterior portion of the left thigh. When the leg was brought backward, the pain complained of was chiefly in the sacral region of the spine. There was no paralysis or paresis of any of the muscles, the limitation of the movements of the left leg was due simply to pain. Reflexes: Knee jerks, both greatly increased; ankle clonus,· absent; plantar reflexes, right fair, left more marked than right; cremaster reflex, right normal, left absent; lower abdominal reflex, absent; epigastric reflex, right present, left absent. Temperature,· localization and muscular senses were all normal. A condition of slight hyperesthesia was found over the left leg, and over the space one-half the size of a quarter on the front of the right thigh there was found the condition of anesthesia. There were no other disturbances of sensation found. Pressure over both ilia at the same time, so as to press the ilia upon the sacrum at the sacro-iliac synchrondrosis, caused considerable pain in the left sacro-iliac joint, and the pain extended from one side of the pelvis to the other. The hip-joint seemed entirely free from pain. There was no tenderness over any of the nerves of the legs.

In the differential diagnosis myelitis, sciatica, hip-joint disease, tumors of the bones of the pelvis, malingering, localized pachymeningitis, and some form of bone disease were discussed. After consideration, all of the above were ruled out except the localized meningitis or the bone lesion. The meningitis if present was considered to be an affection of the external surfaces of the dura, involving the sheaths of the nerves leaving the cord, on only one side, but not involving the cord itself. Now as an external pachymeningitis so rarely occurs in the absence of bone disease, it is fair to presume that we have bone disease and pachymeningitis associated, although it is possible to explain

all the symptoms without the presence of a meningitis. Meningitis, however, would not account for all the symptoms in the absence of bone disease. The pain in the left sacro-iliac synchrondrosis and the tenderness over the first sacral vertebra are due to an affection of the bone or its periosteum.

There is no statement as to the final outcome of the case, although it seems to have been well on the way to recovery when reported.

An accurate pathological diagnosis of the cases here reported is very difficult, and the same difficulty has been met by other reporters of similar conditions. This difficulty is reflected in the titles under which they have reported their cases. Although Gibney had formed a theory that the underlying pathological condition was a perispondylitis, he reported his cases, the first, so far as I know in the literature, under the title, "The Typhoid Spine." Osler, writing later, reports three cases as a neurosis. In the last three years histories of cases presenting certain points of similarity to those reported by American observers have been published in Germany as examples of typhoid spondylitis. While an exact determination of the pathological condition in a disease in which the outcome has been uniformly favorable is practically impossible, the writer wishes to review some of the facts upon which his conclusion is based, that in a certain number of the cases reported the symptoms have been due to an inflammatory process involving one or more of the vertebræ, or their periosteum or cartilages. In so far as I have been able to collect it the literature of the subject consists at present of fifteen articles reporting twenty-one cases, the majority of which I have been able to consult at first hand. I have had access to seventeen or eighteen of the histories of these cases in the report of the observer or in a few instances in a satisfactory abstract. From the standpoint of diagnosis I wish

to call attention particularly to the occurrence of
deformity, and to the frequent association of fever
with the affection.

As to the occurrence of deformity in eighteen
cases, the records are silent on this point in six,
deformity is definitely stated not to have occurred
in six, but in six others there is fair evidence that
a deformity was present at some time in the
course. In three cases, 12, 13 and 14, a kyphosis is
definitely stated to have been observed by the re-
porter. Könitzer,[10] in the introduction to a case
he reports, remarks that a new symptom complex
has been made by Quincke[9] which appears as a
disease of the lumbar and sacral region after ty-
phoid fever, causing very severe pain and swelling
in these parts. This statement leads me to believe
that Quincke's cases, two in number, had some de-
formity. I have not been able to consult his orig-
inal article, and the abstract of the histories of his
cases given by another writer makes no mention of
deformity. In another case[11] the patient claims to
have noticed a prominence in the lower lumbar re-
gion which had disappeared, however, before she
was seen by the reporter. It is well known that
inflammatory processes secondary to typhoid fever
are usually, or at least often destructive, and it is
a rather remarkable fact about these cases, if they
are due to an inflammatory process, that they
have in no case gone on to suppuration, nor does
the deformity usually persist. In five of the cases
in which a deformity was noted it disappeared in
a short time, in one only being present at the time
of the report. Gibney[8] has reported a case of tor-
ticollis in which there was a well-marked deform-
ity of a number of the cervical vertebræ with an
enlargement of their lateral masses in a man of
forty-five who at the age of twenty-two had a
febrile disease of several weeks' duration, pro-
nounced by his physician typhoid fever, and fol-
lowed by a painful affection of the cervical spine.
Gibney reports, also, that a painful affection of

the hip which he observed following an attack of "typho-malarial" fever left some limitation of motion. He mentions these cases as items which strengthen his belief in the correctness of his opinion that the condition is due to a low grade of inflammation. The presence of a febrile reaction associated with the condition under consideration, and not to be explained by any coexisting condition, might, doubtless, be considered, next to the appearance of a kyphosis, the most cogent reason for thinking that the underlying pathological condition was inflammatory. In a total of seventeen cases no statement is made by the reporter in this point in five, in two cases it is stated that no febrile reaction was observed. In the remaining cases, ten in number, the temperature was elevated during some portion of the affection. In two cases slight febrile reaction is reported. In the remaining eight it seems to have reached at least 103° F. at some time in its course. For these and other reasons the writer feels that the true type of the "typhoid spine" is a symptom complex due to an inflammatory process, and that pain in the back following typhoid fever but due to other conditions should not be confused with it. At least one case has been reported [12] in which there was a painful condition of the muscles of the spine, associated with degeneration, leaving behind a contraction of the muscle affected. There have also been observed cases of neurosis apparently not unlike that known as the railroad spine, although in some of these cases it is open to question whether this neurosis was the original condition or a later complication.

The prognosis of painful affections of the spine subsequent to typhoid fever, in so far as recovery is concerned, is excellent. No deaths are recorded in the literature. Even allowing the two cases reported by Gibney, one a painful affection of the cervical spine with permanent deformity, the other a similar painful affection of the hip with

limitation of motion, to influence our prognosis
as to deformity this is also excellent, for in no
other cases in which the course has been ade-
quately followed to determine the final outcome
has any permanent deformity or limitation of
motion been observed. From another standpoint
the prognosis is very different. In very few
cases has the trouble been of short duration. It
has caused a very marked disability for weeks and
more often for months, and in many cases has been
characterized by a series of exacerbation arising
spontaneously or brought on apparently by the
most trivial causes.

In view of the probable duration of a well-de-
veloped case of typhoid spine it seems desirable
to emphasize the necessity for the greatest cir-
cumspection in the management of any case
which during the febrile period or during conva-
lescence, suggests the development of the typhoid
spine by the existence of a weak, aching, painful
back. For a well-developed attack, relief from
pain is the first requirement. This end may be
attained very largely in some cases by rest in a
recumbent position. Additional relief may be
given by various mechanical devices affording ad-
ditional support to the spinal column, as by a
jacket or brace. In a similar fashion, extension
may be serviceable. Later a jacket may be of
further assistance in supporting the back, in reas-
suring the patient and in permitting him to get
about at an earlier date than would otherwise be
possible. For the relief of pain also antirheu-
matic, sedative and hypnotic remedies may be
employed, but unless the suffering is mild, opiates
will be found necessary, from time to time, to
make the patient's condition bearable. The use
of nourishing food and of tonics will be indicated
at appropriate times. Other medication seems
not to be of any great value, although potassium
iodine has been used in a number of cases with
apparent benefit.

## BIBLIOGRAPHY.

1. Gibney. The Typhoid Spine. New York Medical Journal, 1889, i, 596-598. Reports three cases; also one of an acute, extremely painful affection of hip, bearing the same relation to the fever as did the affections of the back, and a fourth case in all probability of different nature as pointed out by Osler. Discusses probable pathology of the affection. The literature of bone lesions in typhoid, etc.
2. Fussell. The Typhoid Spine. New York Medical Journal, 1898, i, 635. Reports one case.
3. Gibney. A Further Contribution to Typhoid Spine. University Medical Magazine, Philadelphia, 1891, vol. iv, No. 2, p. 32. Reports case of torticollis, said to have originated after an attack of typhoid fever occurring twenty-three years previously. Reported for its bearing upon the pathology of the affection. Mentions the fact that a slight impairment of motion has persisted in the hip alluded to in first communication.
4. Eskridge. Periostitis of the pelvic bones following typhoid fever. Kansas City Medical Index, January, 1893. Reports one case.
5. Osler. On the Neurosis following Enteric Fever known as the Typhoid Spine. American Journal of the Medical Sciences, Philadelphia, 1894, N. S., cvii, 23-30. Reviews cases of Gibney's original article. Refers to possible case and reports two others.
6. Study. The Typhoid Spine. Medical Record, New York, 1894, xlvi, 109. Reports one case.
7. Romme. Le "Typhoid Spine" et les neurosis post-typhiques. Gaz. hebd. de méd., Paris, 1894, xii, 562-564. Reviews Osler's article, Summary of Gibney's and of Osler's cases.
8. Newcomet. A Case of Typhoid Spine. International Medical Magazine, Philadelphia, 1898, vii, 597-599. Discusses the subject with references to literature. Reports one case.
9. Quincke. Ueber Spondylitis Typhosa. Mittheil aus den Grenzgeb., 1899, Bd. iv, H. 2. Reports two cases.
10. Könitzer. Ein Fall von spondylitis typhosa. Münch. Med. Woch., 1899, p. 1145. Reports one case.
11. Schanz. Ueber Spondylitis Typhosa. Arch. f. klin. chir., Bd. lxi, H. 1. Gives history of two cases reported by Quincke and of one by Könitzer. Reports one case.
12. Neisser. Exact title not known. Deutsch. Aerzte Zeit., 1900, H. 23. Vergl. ferner. herz. Zeitschr. f. Orthop. Chir., Bd. viii, No. 1. Reports two cases.
13. Kuhn. Ueber Spondylitis Typhosa. Münch. Med. Woch., 1901. Gives histories of cases reported by Quincke, Könitzer, Schanz and Neisser. Reports one case.
14. Taylor. The Typhoid Spine. Philadelphia Medical Journal, vol. viii, No. 26, p. 1134. Reports one case.
15. Crittenden. Salient Points in an Epidemic of Typhoid Fever Based upon Fifty-five Cases. New York Medical News, 1901, vol. lxxix, No. 1, p. 12.

*6*

# REPEATED COPIOUS HÆMOPTYSIS FROM AN AORTIC ANEURISM, EXTENDING INTO THE RIGHT LUNG AND FINALLY RUPTURING INTO THE PLEURA.[1]

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The case I wish to report is that of J. McD., an Irishman, [98] 39 years of age, who was admitted to the Lakeside Hospital, Medical Number 4303, in the service of Dr. Edward F. Cushing, on July 13, 1904, complaining of pain in the right upper chest, cough, and expectoration of blood. His father had died of consumption. Beyond this the family history was negative. The patient had always been a healthy, strong man, by occupation a laborer, and had done hard work all his life. He had rheumatism twelve years ago, and slight attacks of the same disease ever since then. As to specific history, the patient admitted having gonorrhœa three times, the last attack eight years before, and a soft chancre eighteen years ago. No history of a primary sore or secondary syphilitic lesions could be obtained. Except for the minor diseases of childhood, the patient had had no further illnesses. He used alcohol to excess.

The patient dated his present trouble from a year before admission to the Hospital, when he began to have discomfort in his chest, especially the right front, shortness of breath,

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[1] Read before the Clinical and Pathological section of the Cleveland Academy of Medicine, on Nov. 4, 1904.

[98] dizziness, ringing in the ears, and attacks of weakness. His general condition grew worse until two weeks before admission to the Hospital, when he began to cough and expectorate small amounts of blood. At this time, the pain in the chest grew much more severe, and on admission it extended to the right shoulder and down the right arm to the elbow. On the day he came into the hospital, he had had an especially profuse hæmorrhage, but was quite indefinite as to the exact amount. During the past year, he had lost twenty pounds in weight.

On examination, the patient was found to be a well built, muscular man, coughing frequently and expectorating considerable quantities of blood-stained mucus. His voice was husky but not brazen, and the cough not the typical " goose cough." His respirations were normal, the pulse regular and of good volume, 88 per minute. The left pulse seemed slightly more full than the right. They were synchronous. The face was of good color; pupils equal and normal; slight arteriosclerosis. There was a very slight tracheal tug. On inspection of the chest, it was found to be symmetrical and the expansion equal. Over the first and second right inter-spaces, for a distance of 11 cm. from the mid-line and over the third inter-space for 4 cm., there was a marked visible pulsation, [99] but no bulging of the chest. On palpation over the pulsating area a slight systolic impulse could be felt, followed by a marked diastolic impact. There was no thrill. On percussion, dullness was obtained in this region over an area of 11.5 cm. laterally, and 9 cm. vertically downward from the right clavicle. The dullness did not extend to the left of the sternum. In the right back, the dullness extended from a point 3 cm. above the angle of the scapula upward for 8 cm., and included the entire space between the spinal column and the scapula. No pulsation or tumor was noted in the back. On auscultation over the right upper chest could be heard a markedly accentuated diastolic shock, and a loud friction rub, synchronous with the respiration. No bruit was audible. The lungs were elsewhere normal.

The apex of the heart was slightly more to the left than normal, in the fifth interspace 10.5 cm. from the mid-line, and the cardiac dullness 13.5 cm. out, or 4 cm. outside of the

nipple. Except for a marked increase in the intensity of the
aortic second sound, the heart sounds were normal. The phy-
sical examination was otherwise negative.

The unquestioned diagnosis of aneurism of the thoracic
aorta was made, and the attempt made to put the patient on a
modified Tufnell treatment. He, however, objected so ser-
iously to the dry diet, and so absolutely refused to remain
quiet, that this had to be given up. For ten days everything
went well. After the second day, the bleeding stopped, and
the cough and pain were greatly relieved. On July 23, how-
ever, after a sudden movement, the patient commenced cough-
ing, and spat up four ounces of almost pure red blood. This
was the beginning of a remarkable series of sixteen hæmor-
rhages. The next was on July 29, 8 ounces, and from then
they occurred as follows: August 2, 12 ounces; August 6,
32 ounces; August 9, 16 ounces; August 11, 36 ounces; Au-
gust 17, 16 ounces; August 20, 6 ounces; August 21, 20
ounces; August 24, 28 ounces; August 28, 10 ounces; Sep-
tember 2, 4 ounces; September 3, 2 ounces; September 5,
16 ounces; September 13, 8 ounces; and September 14, 7
ounces; in a period of seven and a half weeks a total of 225
ounces or slightly over 14 pints. This was almost pure blood,
mixed with very little mucus. The hæmorrhages in each
case, coming on after some exertion, as sitting up, or reaching
for an article on the floor, lasted only a very few minutes,
and accompanied paroxysms of coughing. At no time did he
raise any fibrin or blood-clot. The hæmorrhages were in each
case stopped by morphia, at times as much as a grain being
required. The patient became steadily more pale. The red
blood count dropped from 4,864,000 to 2,304,000 and the
hæmoglobin from 65 per cent to 38 per cent in the first month
after which, owing to an accident to the hæmoglobinometer, no
record could be taken, but from the patient's appearance, it
must have been much below this. Two days after the last
hæmorrhage on September 15, 1904, the patient during a fit
of anger, suddenly sat up in bed, became very weak, broke out
into a cold sweat, and said he was dying. The pulse rose from
60 to 125 but remained fairly strong. The respirations be-
came labored and finally stopped, the heart continuing to beat

[99] for some time after this. The patient died in about twenty minutes. During the last few days of the patient's life, signs of fluid were evident in his right chest, causing flatness at the base. The probable size of the aneurism and the danger of puncturing it made it seem inadvisable to use the exploring needle. Several attempts were made to examine the patient's larynx, but no good view could at any time be obtained.

During the illness, it was a matter of much speculation among the attending physicians why an aneurism, with a perforation large enough to cause such repeated large hæmorrhages, should stop bleeding at all, and not cause an immediate lethal hæmorrhage. The explanation of this is perhaps found in autopsy findings for the records of which, and for aid in summarizing the same, I wish to thank Dr. William T. Howard, Visiting Pathologist, and Drs. D. H. Dolley and J. H. Bacon, Resident Pathologists of the Lakeside Hospital.

<center>AUTOPSY REPORT.</center>

The following abstract is taken from the autopsy protocol:

Autopsy by Dr. David H. Dolley, September 16, 1904, aut. No. 536. The body is that of an adult male, 170 cm. long. Rigor mortis marked. Pupils equal and dilated. The chest is flat, the supra- and infra-clavicular fossæ well marked. There is no bulging or other abnormality of the thorax. The abdomen is scaphoid. The extremities are free from wounds, scars, and deformities. The superficial glands are not palpable.

*Thorax.*—The sternum, ribs, and costal cartilages are normal. The left lung over-laps the heart to more than the usual degree. The upper lobe of the right lung is the seat of a rather firm mass. The middle and lower lobes are not visible. The right pleural cavity contains 3000 cc. of dark blood-tinged fluid containing flakes of fibrin. The right parietal pleura is smooth and free from adhesions. The left pleural cavity contains a small amount of clear fluid. The pleura is smooth and free from adhesions. The thoracic contents were removed en masse.

*Heart.*—The pericardial cavity contains 200 cc. of clear fluid. The parietal layer of pericardium is somewhat thick-

<center>(4)</center>

ened, as is the visceral layer over the right ventricle. At the
latter point, the epicardium is red and rough. The peri-
cardium is adherent to the upper lobe of the right lung, over
the surface of which it extends for a considerable distance.
The heart muscle on section is pale and flabby. The segments
of the mitral valve are moderately thickened. The segments
of the aortic valve are normal in appearance and show no
thickening. The tricuspid and pulmonary orifices are of
normal size and appearance. The right auricle is markedly
compressed by the aneurism to be mentioned later. All the
valves are apparently competent.

*The Aorta.*—The aorta just above the valve measures 7.5
cm. in circumference, at the junction of the ascending and
transverse portions of the aorta, 8 cm. Below this, the vessel
is not dilated. The aorta throughout is the seat of a number
of large and small irregular thickened areas, which project
slightly into the lumen. Some are calcified and rough. The
large branches of the aorta are normal. On the right side [100]
of the aorta, 3 cm. above the valve, there is an oval open-
ing, 2.5 by 1 cm. in diameter, leading into a spherical sac,
9 cm. in diameter, which is filled with laminated fibrin, the
superficial layers of which, are soft and of a grayish-red color,
while the deeper layers are white and firm. The opening of
the sac into the aorta is partly closed by a rather firm mass of
grayish-white thrombus. This aneurismal sac, which is round
in outline projects upward and somewhat backward, directly
into the upper lobe of the right lung, which incases it through-
out two-thirds of its extent. Anteriorly the sac is adherent
to, and is covered, to a considerable extent, by somewhat
thickened pericardium. The walls of the aneurism are com-
paratively thin, being thickest at the base, where they average
8 mm. and thinnest at the point just opposite the opening into
the aorta, at which point the walls are lost in the lung tissue.
Over a large part of its extent, the walls of the sac and the
visceral pleura are continuous. Microscopically, the wall con-
sists of firm fibrous tissue, organising fibrin and inflamed
pleura, with occasional scattered traces of markedly com-
pressed alveoli. At the point directly opposite the commun-
ication between the aorta and the aneurismal sac, there is

[100] an opening between the latter and the pleural cavity. At this point, the pleura is ruptured, and a rough mass of grayish-red fibrin projects into the pleural cavity. This opening is a linear tear, 5 cm. long. Adherent to the upper lobe of the lung, near this point, there is a fresh blood clot, weighing 700 grams. On transverse section through the sac and the right lobe, the whole interior of the sac is filled with, at some places firm, and at other places friable, clot. The aneurism occupies nearly the whole of the upper lobe of the right lung, and two-thirds of the extent of the aneurism is situated in this lobe. The bronchi leading to the upper lobe contain no blood, but on section, small bronchi can be traced into the aneurism sac. The lower and middle lobe of this lung are collapsed, airless and rather firm. The pulmonary arteries are normal throughout.

*The Left Lung.*—The left lung is voluminous and markedly emphysematous. On section, it is œdematous throughout. The bronchi of both lungs, the trachea, and larynx are normal in appearance.

*Abdomen.*—The abdominal muscle and subcutaneous tissue are normal. The diaphragm on the right side projects 4 cm. below the costal margin. The liver is displaced downward and to the left, and reaches a point 5 cm. below the umbilicus, the right lobe lying directly in the middle line. The stomach is displaced downward into the left iliac fossa. The ileum and jejunum and the transverse colon are displaced into the pelvis. The other abdominal organs are in their usual positions. The abdominal cavity contains a moderate amount of clear fluid. The peritoneum is smooth and free from adhesions. The liver is of ordinary size and shape. The biliary system is normal. The spleen, kidneys, pancreas, stomach, intestines, and other organs show no pathological changes.

*Anatomical Diagnosis.* Arterio-sclerosis of the aorta with sacular aneurism of the ascending arch of the aorta, projecting into and occupying a greater portion of the upper lobe of the right lung. Compression atelectasis of the right lung. Ruptured aneurism and extensive hæmorrhage into the right pleural cavity. General enteroptosis. Pressure upon the right auricle. Oedema and chronic passive congestion of

both lungs. Hydro-thorax, hydro-pericardium, and hydro- [100] peritoneum. Communications between aneurism and small bronchi.
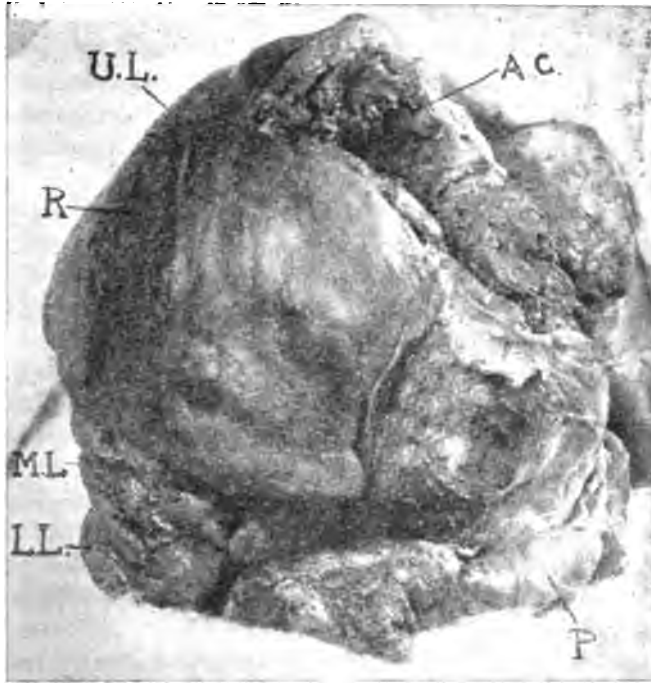


RIGHT LUNG SHOWING ANEURISM.

U. L. = Upper Lobe and aneurism. M. L. = Middle Lobe. L. L. = Lower Lobe. A. C. = Aneurism Cavity opened. R. = Rupture. P. = Pericardium.

## LITERATURE.

The point of especial interest raised by this case is that of non-lethal hæmorrhages in cases of thoracic aneurism. After looking up with some care, all the literature available in Cleveland, I have been compelled to conclude that such cases are very rare. Though cases have occurred, in which one or two severe hæmorrhages have been followed by months or even years of exemption, I have not found reference to any such series of large hæmorrhages as are here reported. With the

[100] facilities at my disposal, I have been unable to make a complete review of the literature, but have collected six cases showing one or more points of similarity to the present one.

In 1847, the case of the English surgeon, Mr. Liston was reported. This gentleman, after one profuse hæmorrhage, was absolutely well for three months. Then, after two months in which he steadily failed, and expectorated considerable rusty sputum, he died, without further hæmorrhage. At autopsy were found three old perforations into the trachea, blocked by blood clot. (1)

Gairdner, in 1859, reported a case in which the patient was ill ten years. Four years before he died, he had two profuse
[101] hæmorrhages from his lungs, followed by some staining of the sputum. After this, he had no more hæmorrhages, though for the last six months, some staining, until a hæmorrhage of eight ounces caused suffocation and death. The autopsy revealed an aneurism of the descending aorta which had perforated the left bronchus and trachea, the perforation being filled with old clot. The left lung was collapsed but not involved. (2) Gairdner also states that up to that time, 1859, nine cases of thoracic aneurism had been reported which had had hæmorrhage two months or more before death. He gives no references except to the case of Mr. Liston, and I have been unable to find these cases.

Two cases are reported by Dr. Osler somewhat similar. The first, in which the patient had a hæmorrhage of two quarts and three weeks later slight hæmoptysis, Dr. Osler reports eight months later as a cured aneurism. (3) The second is a man, who, after one profuse hæmorrhage, lived four weeks, and then dropped dead without further bleeding. At autopsy, this case was very similar to the one here reported. It was an aneurism of the ascending arch, a large part of the wall of which was made up of pulmonary tissue, the trachea not being involved. In this case, as in the present one, death followed perforation of the aneurism into the right pleural sac, with internal hæmorrhage. (4)

Peacock reported in London still another case where the descending arch was involved, the aneurism wall being composed of the upper lobe of the left lung. This case spat up

small amounts of blood for some time and finally died from
rupture into the left pleura. (5)

Involvement of the lung in aneurism is a comparatively rare
occurrence, but is one thing to be thought of in the considera-
tion of pulmonary hæmorrhage, especially where there is a sus-
picion of thoracic aneurism. That an aneurism may cause
extensive destruction of lung tissue without hæmorrhage is
shown by Johnson's case. In this, the patient had symptoms
of chronic pleurisy, and had no hæmorrhage until the fatal
one. Aneurism was not suspected, but at autopsy one was
found, of the descending aorta involving the lower left lobe of
the lung, the aneurism walls being only one quarter of an
inch thick, composed of fibrin, indurated lung and pleura.
(6) This of course, must have existed for some time, but the
bronchi were presumably compressed and obliterated in the
wall of the sac.

From the above cases it would appear that, while hæmop-
tysis is a common fatal termination in thoracic aneurism,
a very large hæmorrhage may occur in this disease, without
causing the death of the patient, and that occasionally a pa-
tient may have one or more large hæmoptyses, and finally die
from some other complication of the aneurism. The point of
bleeding may be from rupture into the trachea or bronchi and
be stopped by the opening being plugged with fibrin, or it may
occur from involvement of the lung tissue itself. In the latter
case, it is probable that the small bronchioles open into the
wall of the sac, but are so compressed by it, that they normally
remain closed, or are covered by fibrin. On exertion, or mov-
ing, either the fibrin shifts its position, or the straining of
coughing opens the ends of the small bronchi and the blood
leaks out. On the patient again becoming quiet, either nat-
urally or by means of narcotics, the original condition is re-
sumed and the bleeding is temporarily arrested.

In closing, I wish to express my thanks to Dr. William Osler
of Baltimore, for some useful suggestions and for information
concerning his cases, and to Dr. Edward F. Cushing of Cleve-
land for permission to report this case from his service at
the Lakeside Hospital.

BIBLIOGRAPHY.

(1) Lancet, London, December, 1847, p. 633.

(2) Trans. Roy. Med. and Chir. Soc., London, 1859, p. 189.

(3) Phila. Med. Times, 1888, XIX, p. 149. .

(4) Ibid., 1889, XIX, p. 223.

(5) Trans. Path. Soc., London, 1863, XIII, p. 39.

(6) Lancet, London, January 12, 1867, p. 44.

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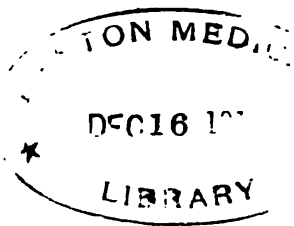
# Hydrophobia with Report of Three Cases.

## BY HENRY S. UPSON. M. D.,

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OF the three cases which I wish to report tonight, two occurred under my own observation in 1899, and the third is of recent occurrence in the practice of Dr Thomas Hubbard of Toledo, who kindly allows me to report it with my own.

The first patient, Mr L., 71 years of age, was seen at the request of Drs J. F. and W. S. Hobson on May 30, 1899. Until the development of this difficulty he was in good health. During the very cold weather early in February he went to the barn to milk, and was bitten on the hand by a large tomcat, which sprang upon him without obvious reason. He had been in the habit of petting the cat, which seemed to be fond of him. He allowed about one-half hour to elapse, and the wound was then cauterized and treated with an antiseptic dressing. The cat had been observed to be sick for two or three days previous to this time, was very irritable, wild, and apparently delirious. About three or four days after the bite was inflicted, the cat died. The body was frozen stiff. A rabbit was inoculated from this cat's spinal cord by Dr Perkins, and at the time when the patient was first seen, some four months after the bite, the rabbit, and a cat which had been bitten by the presumably rabid one, were both under observation in the laboratory of the Lakeside Hospital. They were living and well.

The patient was quite well until May 25 when pains began to shoot up from the hand along the arm. This continued for two days. On the 28th the patient was restless, but had a fairly good night's sleep after taking two teaspoonfuls of bromidia and 1/50 grain of hyoscyamin sulphate. When seen by me on the morning of May 30 he had developed considerable difficulty in swallowing. This had been noticed for the first time the night before. It was especially hard for him to swallow water or other fluids. He could not eat any food, although the night before he had eaten a few strawberries and that morning he had eaten two strawberries. He found, however, not much difficulty in taking pills or capsules. In attempting to swallow water he manifested great distress, breathed very fast, sighed deeply, and usually gave it up, although he did manage at times to swallow some fluid. His mind was perfectly clear, he talked rationally, not only on the subject of his illness, but on other subjects, and did not seem very much agitated in view of the circumstances, but was quite sure that he had hydrophobia. The pulse was 100, and the temperature previously taken was also 100°. The pupils were of normal size and reacted well to light. The knee-jerks were both fairly lively, the one on the left side rather the more so. The arteries were considerably sclerosed, and a blowing systolic murmur was heard all over the precordium, most marked over the base of the heart.

When seen again on the same day, at 10:30 p. m., the difficulty in swallowing had markedly increased. The patient was very restless, and attacks of distress and rapid breathing came on frequently without any special cause. The patient still talked rationally, but had eaten nothing during the day, and had evidently grown weaker. A teaspoonful and a half of the bromidia was given with two ounces of milk by the rectum at 11 p. m. At 12: 30 a. m. the patient was not perceptibly better, and was given one-quarter of a grain of morphin by hypodermic. During the night he slept a few minutes at a time, and then would wake in a paroxysm, would jump out of bed and would sometimes insist on going out into the open air. During the night he had grown more and more confused. On the morning of the 31st, he recognized his relatives and friends, but wandered from one subject to another and was decidedly delirious. He staggered markedly when he walked, and had apparently lost in flesh. His pulse was 120. During the night he succeeded in taking a half glass of water by the mouth. After the administration of the bromidia and the morphin, the patient insisted on washing his face and made several attempts to drink water, but without avail. When he washed himself he had fairly severe spasms of the throat muscles, but not more intense than those of the day before.

At four o'clock in the afternoon of the same day the patient was weaker and more delirious. He was in bed, and did not offer to leave it. The temperature had risen to 103° and the pulse was 120. The speech, which, when he was first seen on Tuesday morning showing slight blurring, had become more and more indistinct. This condition deepened during the night, and the patient passed gradually into a condition of muttering delirium bordering on coma. In the morning he was for a time unconscious, and the movements of the hands, legs and face reduced themselves to mere twitchings. The patient at this time was under the influence of morphin. As this passed off he became somewhat more restless and was given another injection. The patient became progressively weaker, and death occurred at 1: 30 p. m. Fairly marked tympanites developed during the night, and 12 or 13 ounces of urine were drawn with the catheter. The urine was of a dark amber color and clear. I regret that it was not examined chemically, but with the excitement consequent on catheterization, which was carried on with great difficulty, it was thrown away. During the night there began to be stiffness of the neck-muscles with a tendency to opisthotonos, and the muscles of the back were also quite stiff. It distressed the patient a great deal to be moved. No paralysis developed in any part of the body. The pupils remained equal and reacted to light throughout the illness.

Two weeks after the patient's death, the rabbit which had been inoculated from the cat's spinal cord died with typical symptoms of hydrophobia of the paralytic variety. Another rabbit was inoculated from the spinal cord of this one, but both this animal and the cat, previously bitten, remained well.

I cannot help regarding this as a typical case of hydrophobia. The patient was an unusually well-balanced man with no hysteric tendency.

While he somewhat feared hydrophobia and was convinced from the very first appearance of his illness that that was what he had, his conclusion was a perfectly rational one well borne out by the facts, and he carried himself throughout with wonderful nerve. With the appearance of such symptoms as he presented only two diseases were possible, hydrophobia and hysteria. The fact that hysteria sometimes simulates hydrophobia is not very significant in view of the fact that it imitates almost every other known disease. I do not myself believe it possible that hysteria can produce an ailment which runs a steadily progressive course and ends fatally within four days. The occurence of muttering delirium passing into coma, not at all of a hysteric type, but much as it is seen in typhoid and other infectious diseases; the elevation of temperature; the stiffness of the muscles of the back and of the neck, with tenderness such as is sometimes seen in meningitis are not, in my opinion, capable of being simulated consciously or hysterically.

The second patient, Mrs. H., 45 years of age, was seen on Saturday, July 8, 1899. For the previous two weeks she had not been feeling well, and on Thursday, July 6, she first noticed that she had some difficulty in swallowing fluids. This developed very rapidly, so that by Friday morning she could swallow neither liquid nor food. When she attempted to do so, she had spasms of the throat-muscles, evinced great distress, and had sighing respiration. She apparently had no idea what was the matter with her, but careful inquiry of her husband at this time developed the fact that two or three months before, in crossing the yard at night, a large black dog had put his front paws on her chest and struck the septum just inside the nares, either with his teeth or with a claw; presumably, from the subsequent illness, with his teeth. There was slight bleeding, but the patient and her friends were not at all alarmed, and paid no attention to the matter. It was practically forgotten. When the patient was seen on Saturday morning, July 8, 1899, she was found to be a fleshy woman of good color. She was sitting in a chair, was spitting thick, tenacious saliva very vigorously in all directions, and was in great distress. This distress was much increased by attempts at drinking, which set up typical spasms of the throat-muscles. At times she would start from her chair, and once or twice fell very heavily. The pulse was 120, soft and quite feeble, and the temperature 107°. The urine contained a moderate amount of albumin, hyalin casts, and a very perceptible amount of sugar. In spite of the fact that she had been given one-half grain of morphin by hypodermic, an hour afterward the pupils were widely dilated and reacted little, if at all to light. In the evening of the same day she was found lying on the couch and tied with a sheet to prevent her from getting up. Her pulse was 140. She had ceased spitting, although she made a few attempts to do so. Her speech, which was somewhat thick when she was first seen, had become a muttering delirium, rather difficult to understand. She was perceptibly weaker. She went into coma, and died quietly at about ten o'clock the next morning. She only made one reference during her illness to the possibility of her having hydrophobia. This

was on Friday evening, and she simply remarked that if she died she did not know what it could be unless it was hydrophobia. This idea was suggested to her apparently by her distress in attempting to swallow liquids, and she made no reference to her experience with the dog.

Physical examination of the thoracic and abdominal organs gave a negative result. The impression made on the observer by the general appearance and demeanor of this patient was not one of fear or of mental distress, but strongly suggested one suffering from an infectious disorder acting on the nerve-centers and the circulation.

The details of the third case are furnished to me by Dr. Thomas Hubbard, of Toledo. The patient was a young man 19 years of age, of excellent health and exemplary habits, employed as clerk in a grain-broker's office. On Thursday, August 29, 1901, he had coryza with some sore throat, for which he consulted his family physician. At that visit he talked with the doctor's wife for some time and to her surprise spoke about dying in a foreboding manner. He was usually very cheerful and hopeful and inclined to reticence. He worked at his desk for two days longer, but on Saturday, August 31, he seemed weak and exhausted. During this interval he had talked with the family about dying, and said that he had pains under his finger-nails and in the shoulder, with some sore throat. On Saturday morning he could not swallow milk, but ate some toast. There was no inflammation to account for the dysphagia. He had convulsions, apparently of hysteric character, at the mention of water, or if he heard it splashing in the room. There was a slightly frothy mucus in the throat which he spat in all directions when having a spasmodic attack. There were throat spasms, and at such times the face became purple. The physician in attendance said that the pulse was not feverish up to Monday evening. At midnight of Monday Dr. Hubbard found the patient with a temperature of 101.1° in the axilla, the pulse 160. The general appearance was that of a hysteric condition rather than that of one in morbid fear of death. The patient watched eagerly every movement, and when he spoke rationally it was only to exaggerate the symptoms mentioned in his presence. He answered questions for the most part rationally. Dr. Hubbard made a careful examination of the throat, larynx and trachea, but found no inflammation and no paralysis. He was given morphin and potassium bromid, and at about 4 o'clock on Tuesday morning he had a convulsion and told his father that he was going to die. The father left the room to call his wife, and the boy was dead when he returned. The body was embalmed within two hours after death, and no autopsy was permitted. No special tests were made to determine whether the death was real or apparent.

On inquiry it could not be learned that this patient had been bitten or in any way infected by a dog. About six months previous to his death, a pet dog belonging to his father was taken sick. The next day the dog went away and stayed all night, returned the next day very sick, and died on the following day without any violent symptoms whatever. The veterinary surgeon who saw him thought that he had been injured internally.

It seems to me that the diagnosis is in this case somewhat difficult. We may, I think, exclude a pseudohydrophobia from fear, as the boy himself never mentioned hydrophobia and his parents say it was not mentioned in his presence. The forebodings of death which he had were such as are found especially in diseases which affect the circulation, notably in angina pectoris. We are left to suppose either a general fear of death, which proved fatal, or the occurrence of some infection which ran a rapid and fatal course. As between hydrophobia and tetanus, the only two diseases suggested in such cases, it seems to me that tetanus may be with great probability excluded, as its symptoms are not present. That the pet dog which died six months ago may have had rabies, and that the rabies may have been in some way transmitted to the patient is a possibility which it seems to me cannot in fairness be overlooked. Rabies of the paralytic form is common in dogs, and usually remains undiagnosed. Infection from such cases is rare, as the tendency to bite is absent, but sick dogs often lick the hand, and it should be remembered that, as Pope says:

"Of all mad creatures, if the learned be right,
It is the slaver kills and not the bite."

It may be well to add a few words on the diagnosis of the disease, in view of the fact that doubt is sometimes expressed by some physicians and many others whether such a disease as hydrophobia exists. Death is the great reality to both doctor and patient, and few diseases which run a progressive and fatal course have their genuineness called in question. Doubt is only made possible by two features of hydrophobia, the one its rarity, the other the fact that its serious manifestations are often obscured by nervousness, the outcome of terror on the part of the patient and others.

In distinguishing clinically between hydrophobia and its hysteric imitation I should be governed by the following considerations: that in the real disease the symptoms develop gradually; that delirium is not of sudden onset and early appearance but occurs some time after the appearance of the spasms in the throat; that together with the delirium come the signs of nerve exhaustion, the rapid pulse and often fever which usually accompany acute infectious diseases. In a well-marked case the clinical picture is as convincing as is that of typhoid fever. Death occurs in a way little if at all suggestive of exhaustion from fear, but seems to come as an overwhelming of the nerve-centers by a poison essentially depressive after a transitory stage of excitement. The hysteria is as often in the spectators as in the patient. It is easy to mistake chokings and rattlings in the throat for barking, and a calm view of so painful a disease is not to be expected from the friends and

relatives. The delirium of the genuine cases should be distinguished from the hysteria of the spurious ones. Well-marked barking and attempts to bite the bystanders, while they might occur as hysteric additions to the symptom-complex in genuine cases, are strongly suggestive of malingering or of unconscious or hysteric imitation.

It is significant that of the three fatal cases here reported in two of them the fear of hydrophobia was not present. With symptoms so well-marked the prognosis is quite hopeless, and the duty of the physician is to relieve pain and allay distress by adequate doses of morphin. Under the influence of this and other sedatives these patients need not suffer more than do patients dying from many other affections. An early diagnosis is doubly necessary in order that adequate sedatives may be given throughout the course of the disease.

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# The Hereditary Element in Cataract

—BY—

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# THE HEREDITARY ELEMENT IN CATARACT.

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THAT heredity plays an important role in the development of cataract has been known for many years. The literature of the subject, however, is not extensive, not so much so as would seem that the subject would warrant. An occasional instance only of families affected with cataract through two or more generations has been found, a few of these being very striking. Most interesting are the reports of Dyer, Thompson, Dickey, Becker, Green, Berry, Fukala, Fromaget, Arlt and others. In many of these reports the cataracts have been congenital, in some they develop in early life, from three to five or ten years of age, in others in youth, coming on at a certain definite period, in various members of a family, while in still other families the cataracts are always of the senile type. No special form of cataract predominates largely in these various reports which I have been able to examine.

My own experience has to do with at least three families in which the hereditary tendency to the formation of cataract is manifest. It has seemed to me a brief report of these is not without interest. In two of these families, cataracts were present in at least three generations, and in one in two generations. I shall give brief notes of these three families in the order in which they came under my observation.

The first case was that of Garfield M., Æt. 8 years, a well developed boy who had had fairly good vision as a child until about six years old, when his sight began to fail. ·When examined in May, 1888, both eyes showed fully developed cataracts, the entire lens being opaque, of a white color, and uniform appearance. There were good light perception and projection. Early in June, 1888, both eyes were operated upon by discission. The right eye-ball was small, and though operated on more than once, no satisfactory result was obtained, although the pupil was fairly clear, there being evidently some congenital defect, together with a strabismus. The left eye recovered perfectly, with a good clear pupil. Testing the refraction in December, 1888, it was found that with + 16.00 D., V. = $^6/_{15}$. Examined again in August, 1900, it was found that with + 14.00 D., V. = $^6/_6$ +. and with + 18 D., he was able to read any ordinary print with ease. He has been able to go to school with satisfaction, and has performed the work of a farmer perfectly well. With the exception of the eyes, this young man is a well developed, healthy individual in every way.

On August 21, 1900, June M,, Æt. 13, a sister of the above, came to my office with the following history: The sight of the right eye began to fail four years previously, and failed rapidly, so that there was only light perception since. The left eye began to fail three weeks before her visit, and failed so rapidly that within a few days she could see only enough to avoid large objects in walking. At the time of her visit she had only light perception in each eye. The patient was an unusually large, well developed girl in every way. The right eye showed fully developed white cataract, of uniform appearance, while the left showed a less dense lens. The eyes were well formed and apparently in normal condition otherwise. Both eyes were operated upon with needles and with a good clear pupil in each, two operations having been performed on each eye. Practically there was no irritation after either operation, both eyes having been operated on at the same time. After recovery from the operation, testing the refraction gave the following result: O. D. with + 11.00 D. ◠

+ 2.00 D. cy. ax. 90°, V. = $^{6}/_{12}$ +. O. S. with 11.00 + D. ◯ + 3.00 D. cy. ax. 90°, V. = $^{6}/_{12}$ +.

With + 2.00 D. added to the above for bifocals, she has been able to do school and other work with comfort. These two were the only children in this family. On investigation it was found that the mother of these children had cataracts of both eyes as a girl, and had been operated upon success-fully, while the latter's mother gave a similar history of being operated upon as a young girl, also successfully.

The next family which I saw was a Swedish family, living in Ashtabula, Ohio. The first patient seen in this family was Clara W., Æt. 9 months, who was brought to my office on May 13, 1890, having double congenital cataracts. She was a strong, healthy looking baby and in every way well de-veloped. In addition to the cataracts there was convergent strabismus. On May 14, 1890, under ether a needle opera-tion was performed in each eye, the lenses were both quite hard, especially the nuclear portion, so that the needle pene-trated with some difficulty, and the lenses seemed small. There was little reaction afterward. On the 20th, six days later, the eyes were entirely quiet, but the right showed a dislocation of the lens into the anterior chamber. It was thought wise to remove this on account of possible danger from pressure on the iris. On the 22nd of May, under ether, an incision was made upward with a Graefe knife, and the entire lens removed with a wire loop, with no accident. A prolapse of the iris was replaced with the spatula, leaving a clear round pupil. Eserine was instilled, and the eye band-aged. The dressings were all removed on the sixth day, showing a clear round pupil. The patient left for home that day. On June 20th, the left eye was needled the second time, from which the patient made a good recovery.

The second child, Hilda W., Æt. six months, was ex-amined on January 3, 1893, this one also being a well de-veloped baby, with nothing abnormal except the eyes, both of which had congenital cataracts, involving the entire lens. Both of these children were girls, in fact all the individuals affected in this family, so far as ascertained, were females.

The mother of both these children had had double congenital cataracts, operated on in Sweden, and she informed me that she had a sister, who had double cataracts, and had been operated on at six years of age, she dying within six months after the time of the operation.

Dr. Baker has informed me that he operated on the second child, Hilda, of this family when she was five or six years old, successfully. He also informs me that the grandmother of these two children had the same disease and was operated on in Sweden, making therefore, three generations of congenital cataract, with five individuals all affected. There were only the two children in this last generation. So far as could be ascertained all the individuals were strong healthy persons with no other defects.

The third family with cataracts were Germans, the mother being unable to speak much English. Three children of this family, with the mother, appeared at the Lakeside Hospital Dispensary on July 9, 1902. These were Alma H., Æt. 9, Arthur H., Æt. 12 and Ella H., Æt. 15. The following history was obtained: The mother was 44 years old, and had good eyes, the father was 46 years old and had been operated by Dr. Baker five years previously for cataract, first in one eye and then in the other. In this family there were seven children. The first two, boys, had good eyes, while the youngest, also a boy, had good eyes. The other four, three girls and one boy, all had congenital cataracts. The day after the examination of these three, another daughter, Anna H., Æt. 17 years, was brought in showing the same defect. The mother and six of the children were examined by my assistant, Dr. Bruner. Whether the father's was a case of congenital cataract or not it is impossible to say. He had, however, always had poor eyes, and after the operation it was found he had a considerable myopia, together with some choroidal changes. The children had congenital central opacities of the lens, varying somewhat in shape and size, producing greater or less disturbance of vision and incapacitating all of them from doing much reading except with very large type. The vision varied from $3/60$ to counting fingers at

one foot. The eyes were well formed and all the children were large, robust and well developed.

Alma and Arthur were first sent into the hospital and operated upon, one eye at a time. Then all four were sent in and all operated on the same day, one eye in each individual. Up to the present time Alma and her brother have had both eyes operated on, and Ella and Anna have had each one operated on. All of them were successful and none of them had much irritation after any of the operations. The refraction of the eyes after the operation was as follows:

Alma— + 11.00 D. each eye, V. = $^6/_{60}$.

Arthur— O. D. + 6.00 D. $\cup$ + 2.00 D. cy. ax. 60°, V. = $^6/_{21}$ +.

O. S. + 5.00 D. $\cup$ + 2.00 D. cy. ax. 75°, V. = $^6/_{21}$ +.

Ella— O. S. + 7.00 D. $\cup$ + 1.50 D. cy. ax. 105°, V. = $^3/_{60}$.

Anna— O. S. + 10.00 D. $\cup$ + 2.00 D. cy. ax. 90°, V. = $^6/_{30}$.

It will thus be seen that two of the children were somewhat nearsighted. In all of them the pupils were black and clear, and as the tests were made very shortly after recovery from the operations no doubt a careful refraction later on will give better results so far as the testing with letters is concerned. In a sense these patients must learn how to see and interpret. The improvement of vision is well illustrated in the case of the first patient of the series, where after ten or more years his vision had increased, with correction from from $^6/_{15}$ to $^6/_6$ +.

In this series of cases there are reported fourteen individuals, the subjects of hereditary cataract. Of the fourteen three were males and eleven females. In two of the families the line of descent was through females and in one from the father. As to nationality, one was American, one Swedish and one German.

A word as to the operation. There is nothing original in this. For some time I have followed the rule of using a single needle in performing the first operation on cases requiring discission. With this the lens matter itself is pretty well

stirred up, without too extensive damage to the anterior capsule. At the second operation two needles are used. At this time the capsule and lens matter are thoroughly torn apart in the pupillary area. Generally I find that a large portion of the lens matter has been absorbed away after the first needling, and the free tearing of the capsule and remaining lens matter does not produce much reaction, and the patient makes a fairly rapid recovery. As illustrating the results, in the case above of Ella H., she was operated first on March 25th, and left the Hospital on April 6th.' The second operation was on May 28th, and she left well on June 23rd, with almost no irritation after either operation. Anna H. was operated on the same dates as her sister and the recovery was equally satisfactory.

Of especial interest is the case of Clara W., in whom an extraction of the hard nuclear cataract was performed, on account of the luxation of the lens into the anterior chamber, with satisfactory results. The thorough use of atropine I deem of much importance, to be continued until the eyes are absolutely free from all injection. Patients are kept in bed never longer than twenty-four hours, and the eyes are kept covered not longer than four or five days, unless there is some special reason. They are all treated in the open wards, with no darkening of the room or other protection than medium tinted smoked glass.

# WOUNDS OF THE THORACIC DUCT OCCURRING IN THE NECK. REPORT OF TWO CASES. RESUME OF SEVENTEEN CASES.

BY

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Injuries of the thoracic duct may be caused in various ways. They may occur, .first, as the result of diseased processes, such as tuberculosis or malignant growths affecting the wall of the duct ; second, from serious traumatisms, such as fracture of the spinal vertebras; third, they may be caused by accidental wounds of the neck ; fourth, they may arise from division of the duct during operation. Injuries of the first two varieties, so far as have been described, have occurred in the thoracic and abdominal regions, and may give rise to collections of chyle in the thoracic or abdominal cavities. These conditions have been fully described in an article by Kirchmer, and will not be considered further in this paper.

The last two varieties, viz., those which arise from injuries by accident or during operation, occur chiefly in the neck. On account of the anatomic location of the thoracic duct these injuries are, of course, usually upon the left side. With an anomalous arrangement of the thoracic duct, or with multiple branches, it is possible that these injuries may occur upon the right side as well, though no wounds upon the right side have been reported thus far. The immediate object of this paper is to describe two wounds of the thoracic duct which occurred in the surgical service at Lakeside Hospital. The first of these is of very unusual interest. Its history is as follows :

CASE A.—W. D., aged 16½ years. Surgical number 429. Operated on by Dr. Allen. Admitted to hospital October 24, 1898. Tuberculous glands of the neck. Family history good. In April of 1898 he noticed the glands of his neck on both sides began to enlarge. Patient says that he had typhoid fever, being sick from May 30 until July 4, and that after this the glands grew more rapidly, the growth continuing up to the

time of operation. On admission to the hospital the glands on both sides were found to be enlarged. The enlargement was slight upon the right side, but was more marked upon the left. The operation was performed October 27, 1898. By an error, and contrary to orders, the patient had received his breakfast, and the operation was about an hour and a half afterward. An incision was made in the left side of the neck from below the mastoid, parallel to the anterior border of the sternocleidomastoid muscle, down to its insertion in the clavicle. A chain of enlarged glands was removed, and some of them were already cheesy in character. As the dissection approached the lower extremity of the incision it was remarked that one must consider the possibility of wounding the thoracic duct, but that we were so far above it as to be within the line of safety. As nearly as could be estimated, the dissection at this time was between 4 and 5 cm. above the sternoclavicular articulation. While speaking of the matter there was a sudden spurt of grayish-white material, which streamed up into the wound to a distance of between 5 and 7 cm. The force and character of the stream was quite similar to that of blood projected from a wound in a large vein. A sterile sponge was instantly placed over the opening and the dissection completed, all glands so far as they could be found being removed. A very fine needle was then threaded with the finest size of catgut, and with a stitch the opening through which the fluid had escaped was closed. The wound was about 3 mm. long. This was sufficient to completely control the escape of fluid. The upper part of the wound in the neck was then closed by a subcutaneous suture of silkwormgut. A small amount of iodoform gauze was packed over the point at which the fluid had escaped. The gauze was removed upon the third day the wound being perfectly dry. It healed at once without suppuration. The patient was discharged from the hospital on November 11. No fluid escaped from the wound at any time after the operation.

There are several points of special interest in connection with this operation. The first is that the question of wounds of the thoracic duct was being discussed during the operation and the remark being made that the operation was within the bounds of safety. The second factor of interest is that it was not a simple leakage from an undiscoverable wound, but was a stream of good size, spurting up between 5 and 7 cm. into the air. The third point is that the wound was closed at once by a catgut suture and that no subsequent leakage took place, the wound healing by first intention. The size of the stream which escaped may be explained by the fact that the operation was only 1½ hours after a meal, the meal having been given through an error. The character of the fluid was beyond fair question. It was translucent, of a whitish gray color, and presented to the naked eye the physical characteristic of chyle. Unfortunately, none of the fluid was collected for microscopic examination.

CASE B.— V. P., age, 52 years. Surgical number 1,544. Operator, Dr. Allen. Admitted to hospital July 2, 1900. Secondary carcinomatous glands. Family history good. Five years ago the patient was operated on for a carcinoma (scirrhous) of the left breast, the breast being removed and the axilla cleared. For over a year there had been a slight thickening above the left clavicle and the patient had complained of drawing pain in the region of the first operation. Her general health was fair, although not so good as before the first opera-

tion. A few small masses about the size of a pea could be felt above the clavicle on the left side. There was nothing to be felt in the region of the original operation, or in the axilla. The patient was operated on July 3, 1900, having been fully prepared and having had no nourishment for 12 hours. A transverse incision about 10 cm. long was made above the clavicle on the left side, developing the outer edge of the sterno-cleidomastoid muscle anteriorly and the trapezius posteriorly. The omohyoid muscle was divided. A collection of small indurated glands extending well toward the median line were found, and these with the surrounding fat were removed. This was done by first laying bare the subclavian vein and working from this point upward and backward. A small indurated mass of tissue was found posteriorly, under the trapezius, and was removed as thoroughly as possible. There was considerable oozing of blood from the bottom of the wound, but nothing occurred to awaken the suspicion that there had been an injury to the thoracic duct or any of its branches. On account of the oozing the wound was packed with iodoform gauze, this coming out of the center of the incision, while the extremities of the incision were closed with sutures. On July 4, the gauze packing was removed and replaced, there being considerable bloody serous discharge. The patient felt and appeared to be weak. On July 7, the discharge was of a whitish appearance resembling chyle rather than pus. The fluid when examined under the microscope was found to contain a large amount of fat, with a few leukocytes. The fat was very finely subdivided, bearing a resemblance to amorphous urates. It was impossible to collect a sufficient amount of the fluid for more careful examination. By July 15, the discharge had markedly decreased, but as there was an unusual degree of induration about the wound the packing was still continued. By the 21st the discharge had become inconsiderable, changed in appearance, and seemed to come simply from the granulations. At this time the patient was discharged from the hospital in good general condition. A letter from her dated February 28, 1901, says that she is in her usual health.

Following is a report of 17 cases of traumatic injury of the thoracic duct in the neck. Of these, 15 have been the result of operative injury and 2 have been due to accident. They are given briefly in the order in which they were reported:

CASE 1.—Operator, D. W. Cheever. Reported by G. W. Gay.[1] Operation, March, 1875. Male, aged 22 years. Diagnosis, leukocythemia. Tumor of left side of neck. During dissection the subclavian vein and a large vessel in the region of the internal jugular vein were injured, followed by almost uncontrollable hemorrhage. There was also seen flowing from the depth of the wound a transparent, colorless, viscid, coagulable fluid; this escape of fluid was observed half a dozen times, its amount about an ounce at a time. The innominate and subclavian veins were ligated after removing the inner two-thirds of the clavicle. This stopped the hemorrhage completely, but the transparent fluid mentioned still escaped in a moderate amount. Wound tightly packed, no subsequent hemorrhage, only slight staining of dressings with serous discharge. Patient died in 36 hours from "shock and exhaustion." After careful examination through the wound it was thought that the fluid had escaped from a wound of the thoracic duct which could not be located. Patient had fasted for 12 hours before operation. Microscopic examination showed a few blood corpuscles only.

[1] Surgical Operations at the Boston City Hospital. Boston Medical and Surgical Journal, 1875. Vol. 92, p. 422.

CASE 2.—Operator, Wilms. Reported by E. Boegehold.[2] Operation, March, 1880. Male, aged 45 years. Diagnosis, carcinoma. Tumor in left side of neck. Subclavian and external jugular veins exposed. While cureting, a stream of milky fluid was seen about the size of a straw. The wound was packed with salicylate gauze. No subsequent discharge of chyle was seen. The wound healed by granulation. He underwent another operation 6 months later, and afterward died of pulmonary metastases.

CASE 3.—Operator, Maas. Reported by T. Vagedes.[3] Diagnosis, carcinoma. Tumor near parotid, with enlarged cervical glands. Subclavian vein wounded. Wound packed with gauze. During the next 6 days there was considerable discharge of fluid with a sweetish odor. On investigation this was found to come from the bottom of the wound, and was supposed to be from the thoracic duct. The fluid was coagulable. The wound was packed, the discharge ceased, and recovery was uneventful.

CASE 4.—Operator, A. M. Phelps. Reported by W. W. Keen.[4] Operation, June 4, 1893. Male, adult. Diagnosis, malignant tumor. Tumor on left side of neck. During dissection 3 inches of jugular vein were removed with the tumor. Constant profuse discharge of lymph during operation. Subsequent discharge very profuse, estimated at 3 pints a day, saturating dressings and from 10 to 15 folded sheets daily. No mention of packing. Patient lost flesh rapidly. Discharge could be stopped by introducing a knitting needle at point of injury in what appeared to be a vessel. This point was caught with forceps which were removed 3 days afterwards. Patient gained 1 pound a day subsequently, and recovered uninterruptedly. The operator considered it a wound of one of the branches of the duct, but those consulting with him thought it a wound of the duct itself.

CASE 5.—Operator, W. W. Keen. Reported by W. W. Keen. Operation, December 15, 1893. Female, aged 20 years. Diagnosis, tuberculous adenitis. Glands in left side of neck. Difficult dissection, owing to previous operations. Large veins exposed. Lymphatic fluid welled up in wound from a tear ½ inch long in a vessel ⅛ inch in diameter. (Patient had no food for 18 hours previously.) Fluid coagulated on exposure. Opening closed by fine silk suture in finest semicircular Hagedorn needle. There still persisted a slight oozing of similar fluid, but its source from any particular vessel was not traceable. Drainage tube introduced, removed after 5 hours. Discharge through the tube was profuse, being about 1 pint in amount, light in color. Dressings were saturated the next day, after which discharge ceased. Weight unaffected. No mention of packing. Recovery uneventful. Fluid showed lymphocytes, lymph-corpuscles, and many small fat globules. It was slightly opaque.

CASE 6.—Operator, J. Schwimm. Reported by J. Schwimm.[5] Operation, December, 1895. Male, aged 25 years. Diagnosis, tuberculous adenitis. Glands in left side of neck. Incision extended downward to 1 inch above sternoclavicular joint. Glands removed easily and without apparent accident. Ten days after operation slight swelling at lower end of wound, increasing in size to that of a hen's egg. Opened 2 days later, allowing the escape of "a liquid looking very much like

[2] Ueber die Verletzungen des Ductus thoracicus. Archiv für klinische Chirurgie. 1883, B. 29, S. 443.

[3] Ueber Verletzungen des Ductus thoracicus Inaugural Dissertation, Würzburg, 1885. Reference quoted from Cushing.

[4] Operation wounds of the thoracic duct in the neck, with a resumé of two prior recorded cases, and two additional cases. New York Medical Journal, 1894. vol. 59, p. 569.

[5] A case of operative injury of the thoracic duct at the root of the neck. Annals of Surgery, 1896, vol. 23, p. 582.

skimmed milk and showing under the microscope all the characteristics of chyle." The fluid at this time amounted to about 1½ ounces. During the next 2 days the cavity again filled up with about 2 ounces of fluid, and was then packed with iodoform gauze, after which the discharge of chyle increased greatly, amounting to 1½ to 2 pints in 24 hours. This soon resulted in constitutional effect, and a few days later the patient was removed to a hospital, the lower end of the wound opened, and a small vessel readily found from which chyle was escaping; this vessel had been torn through, the opening being about the size of a knitting needle. The vessel was clamped, the clamp remaining on 3 days. The condition of the patient began to improve immediately and recovery was complete.

CASE 7.—Operator, C. A. Porter. Reported by H. W. Cushing.[6] Operation, December, 1897. Diagnosis, tuberculous adenitis. Glands in left side of neck. Duct reached 4 cm. above the subclavian vein. Wound of duct ½ inch above entrance into vein caused the escape of a clear yellowish fluid at the rate of about 1 to 2 drams in 10 minutes. Wound repaired with 3 fine Lembert sutures. There was still a slight discharge of lymph which was thought to come from a small radicle. Wound opened on the second day, discharged 15 days. No constitutional effect. Recovery complete.

CASE 8.—Operator, W. S. Halsted. Reported by H. W. Cushing. Operation, November 5, 1895. Female, age 66 years. Diagnosis, carcinoma. Tumor of left breast with enlarged axillary glands. Complete excision of breast, pectoral muscles, axillary and supraclavicular contents. Wound healed by first intention. Ten days after operation wound above clavicle opened, and 4 or 5 ounces of milky fluid evacuated. Gauze drainage introduced, following which there was profuse discharge for 8 days. During this time the patient lost 10 pounds. Wound explored, discharge observed coming from level of omohyoid muscle where it crossed the jugular vein. Gauze packing introduced. No subsequent leakage. During the next 15 days patient gained 23 pounds. Subsequent recovery uneventful. Died in 1896 of internal metastases.

CASE 9.—Operator, H. W. Cushing. Reported by H. W. Cushing. Operation February 25, 1898. Female, age 62 years. Diagnosis, carcinoma. Recurrent supraclavicular glands on left side, following excision of left breast 2 months previous. During dissection the thoracic duct was wounded about 1 cm. above the subclavian vein. The vessel extended 4 cm. above its entrance into the vein. "A large branch, about the size of the usual silver probe, entered into this vessel just below the point of injury, and disappeared behind the subclavian about 2 cm. to the left of the main duct." Wound 3 mm. long, allowing intermittent flow of considerable clear serous fluid. Wound in duct closed with fine silk Lembert suture; no subsequent leakage. Wound closed; recovery uneventful. Writer claims first case of suture without leakage.

CASE 10.—Operator, W. H. Lyne. Reported by W. H. Lyne.[7] Operation May 5, 1896. Male, aged 24 years. Diagnosis, stab wound in neck, left side. Bleeding had stopped when patient was seen. There persisted, however, an abundant milky fluid discharge. The wound was 1 inch long behind the left clavicle, parallel with the outer border of the sternomastoid, near its attachment, "necessitating a longitudinal wound of the thoracic duct." Wound cleaned, and packed with iodoform gauze; repacked 7 hours later, when discharge was found to have ceased. No subsequent leakage. Recovery uneventful. No examination of fluid reported.

[6] Operative wounds of the thoracic duct. Report of a case with suture of the duct. Annals of Surgery, 1898, vol. 27, p. 719.
[7] Stab wound of the thoracic duct, recovery. Virginia Medical Semi-Monthly, 1898, vol. 3, p. 278.

CASE 11.—Operators, W. E. Schroeder and S. C. Plumber. Reported by W. E. Schroeder and S. C. Plumber.[8] Operation, date not given. Male, aged 24 years. Diagnosis, not given. Cystic tumor at base of neck on both sides. During dissection on left side the internal jugular vein was injured and ligated. Escape of lymph " was seen to come from small orifice, evidently an opening in a large lymphatic vessel, either in the thoracic duct itself or its large subclavian branch." Attempts to ligate the vessel were unsuccessful; no attempt at suture was made. " From the horizontal position of the vessel it was taken to be, most probably, the large subclavian branch of the thoracic duct." Discharge at operation was transparent, yellowish, and not excessive. Wound packed with iodoform gauze; slight serous discharge for 3 weeks. Recovery otherwise uneventful.

CASE 12.—Operators, W. E. Schroeder and S. C. Plumber. Reported by W. E. Schroeder and S. C. Plumber. Operation, date not given, Female, aged 23 years. Diagnosis, tuberculous adenitis. Glands in left side of neck. During the operation a milky fluid was seen to escape from " an injury to the thoracic duct, or one of its large branches." The vessel was found and lifted with forceps. Air was inspired through the wound. " The vessel was ligated," but chyle still discharged through a small opening, " which was also ligated." No subsequent leakage. Recovery uneventful, except for slight rise of temperature for a few days following operation.

CASE 13.—Operator, F. B. Lund. Reported by F. B. Lund.[9] Operation, December 18, 1898. Female, aged 34 years. Diagnosis, carcinoma. Tumor in left breast. Excision of left breast with axillary and supraclavicular contents. Internal jugular and subclavian veins dissected out. Thoracic duct sought, but not found. No lymphatic injury suspected at operation. Four days after, cervical wound opened and a " partially coagulated milky fluid" evacuated. The leakage was found to be quite brisk, requiring a change of large dressings every 3 hours. This continued for 4 days. The wound was packed lightly with gauze without effect, but subsequent firm gauze packing stopped the discharge. Convalescence uneventful. No constitutional effect mentioned.

CASE 14.—Operator, J. C. Warren. Personal communication.[10] Operation, 1896. Female, age not given. Diagnosis, carcinoma. Recurrent supraclavicular glands 2 years after first operation. No injury of the thoracic duct was observed at the time of operation, but 5 days afterward, a fluctuating tumor about the size of a Messina orange was evacuated. Discharge continued from 1 to 2 weeks, but was finally stopped by a graduated compress held in place over the wound by a strip of adhesive plaster. The character of the fluid was not mentioned, other than that it was " chyle." A similar operation was performed one year later, and the same occurrence took place. Patient died of internal metastases in 1898. The case was published in Dr. Warren's cases of cancer of the breast, but no allusion was made to the injury of the thoracic duct.

CASE 15.—Operator, A. Münter. Reported by A. Münter.[11] Operation, June 16, 1898. Male adult. Diagnosis, incised wound at base of neck, on left side, caused by a blow from an axe. The patient had bled a considerable amount, and was pale and weak. The wound had been dressed temporarily with

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[8] Report of two cases of injury of the thoracic duct in operations on the neck. Annals of Surgery, 1898, vol. 28, p. 229.

[9] A case of operative injury of the thoracic duct. Boston Medical and Surgical Journal, 1899, vol. 140, p. 354.

[10] Also mentioned by F. B. Lund and J. C. Warren, at a meeting of the Surgical Section of the Suffolk District Medical Society, January 4, 1899. Boston Medical and Surgical Journal, 1899, vol. 140, p. 353.

[11] Schnittverletzung des Ductus thoracicus. Deutsche medicinische Wochenschrift, 1899, No. 48, p. 799.

horse dung, which was a favorite means of stopping hemor-
rhage in that community. The wound was 12 cm. long in the
left supraclavicular fossa, reaching the clavicle, and dividing
the clavicular attachment of the sternomastoid muscle. The
external jugular vein was divided. From the depth of the
wound a milk-white stream about the size of a straw was flow-
ing from a small vessel which was thought to be the thoracic
duct. No attempt at ligating the vessel was made, as conveni-
ences and assistants were not at hand. The wound was cleaned
and packed with iodoform gauze, securely bound down, and the
patient sent to a neighboring hospital. The next day the wound
was opened and the chylous discharge continued. The vessel
from which it was escaping was readily ligated, the divided
sternomastoid muscles sutured, and the wound closed. There
was no further discharge, and recovery was uneventful.

CASE 16.—Operator, D. P. Allen. Reported by D. P. Allen
and C. E. Briggs. Case A, reported in full above.

CASE 17.—Operator, D. P. Allen. Reported by D. P. Allen
and C. E. Briggs. Case B, reported in full above.

A number of these cases have been collected pre-
viously. Cheever, Case No. 1, 1875, is the first report
found. Boegehold, in reporting his case, No. 2, 1883,
made no mention of Cheever's case, although he appears
to have searched for previous instances. Keen's report,
1894, included the cases of Cheever and Boegehold, to
which he added the case of Phelps, No. 4, and his own,
No. 5. Cushing, 1898, again reported the four cases
mentioned by Keen, collected in addition the cases of
Vagedes, No. 3, Schwimm, No. 6, and added the pre-
viously unreported cases of Porter, No. 7, Halsted, No.
8, and his own, No. 9. To these are now added the
collected cases of Lyne, No. 10, Schroeder and Plumber,
Nos. 11. 12, Lund, No. 13, Warren, No. 14, Münter, No.
15, and the report of two new cases, Nos. 16 and 17.
This last series includes the only two reported cases of
accidental (nonoperative) wounds of the thoracic duct
in the neck, Cases Nos. 10, 15, both of which, however,
were handled in the same manner as operative wounds.

Information contained in the standard textbooks of
surgery on the injuries of the thoracic duct is very
meager and with reference to injuries of the duct in the
neck there is practically nothing. One looking for
information, therefore, is obliged to go to a good many
sources. Boegehold, in 1883, was the first to give any
detailed consideration of the subject. He was followed
by an admirable article by Kirchner in 1885.[12] Both of
these writers, however, approach the subject from the
standpoint of wounds of the thoracic duct in general and
say practically nothing with reference to cervical wounds
of the duct. Keen, in 1894, was the first to give any
detailed consideration of cervical wounds of the duct.
Cushing, in 1898, supplemented Keen's considerations
by a slightly more extended report. As the number of

[12] Ein Fall von rechtsseitigen Chylothorax in Folge von Ruptur
des Ductus thoracicus, nebst Statistik und Kritik der bisher bekannten
einschlägigen Fälle, Archiv für klinische Chirurgie, 1885. B. 32, S. 156.

reported cases, however, has been nearly doubled since 1898, and as a number of points have arisen for consideration which had been previously disregarded, it seems permissible to add somewhat extensively to the work already done, even at the risk of a certain amount of repetition.

*Anatomy.*—The anatomy of the thoracic duct is of importance in this connection, with reference to two considerations: First, the relations of the duct in the neck with reference to preserving its integrity in low cervical dissections; second, the anatomic distributions of the duct commonly spoken of as its anomalies, through which collateral circulation may take place in case the duct is irreparably injured. What is considered the normal course of the duct in the neck is described in the standard works on anatomy as the course taken between the esophagus and the left subclavian artery, reaching as high as the lower portion of the seventh cervical vertebra, curving over the apex of the pleura and the left subclavian artery, and terminating in the outer side of the angle formed by the internal jugular and subclavian veins. In taking this course its highest point is about 3 to 3.5 cm. above the upper margin of the sternum, but lying as it does to the inner side of the arch of the left subclavian artery, it is so deeply placed in the neck that there is seldom danger of injury, although its height above the sternum is considerable. Nevertheless, a number of instances have been observed in which the arch of the duct has reached considerably above the point mentioned, and an instance is mentioned [13] in which the arch of the duct was 5.5 cm. above the sternum, reaching the thyroid gland. In the case of Cushing, No. 9, and Porter, No. 7, the duct was 4 cm. above the innominate vein, and in Case No. 16 reached about 5 cm. above the sternum. Keen, Case No. 5, does not mention the height of duct above the vein, but it was probably abnormal, as the vessel itself was injured in open dissection. It seems probable that operative wounds of the main duct have occurred only in instances of abnormally high arch, and that the other wounds mentioned have been injuries of some of the radicles only.

With reference to the anomalous distribution and ending of the thoracic duct, marked variations have been observed. They are of practical interest only so far as they tend to strengthen the belief in adequate collateral circulation following injury of the duct itself, or one of its branches. Without going into extensive details, the following variations may be mentioned: A double duct entering the innominate vein on both sides of the neck; a duct entering the vena azygous major, the lumbar or vertebral veins, or the vena cava; a duct

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[13] Henle's Anatomy, 1876, vol. 3, p. 458.

entering the right internal jugular or right innominate
only, which condition, however, is usually associated
with an anomalous right subclavian artery or a right
aortic arch. The number of cases of multiple termina-
tions of the duct in the left internal jugular, the subcla-
vian and innominate veins are too numerous to record,
and it seems probable that subsequent careful observa-
tions will confirm the opinion that in a considerable
proportion of cases such multiple terminations exist.
From an anatomic standpoint, therefore, the probability
of adequate collateral circulation after injury to one of
the large terminal branches of the duct seems extremely
strong, and as injuries of the main duct itself occur so
near its entrance into the vein, it seems quite likely that
satisfactory collateral circulation would follow in such
instances.

Histologic features of the duct have a practical value
relative to the contraction of the duct following injuries.
In general the structure resembles that of the artery,
with an intima, a muscular media, and connective tis-
sue adventitia. The striking difference, however, is the
abundant distribution of elastic fibers through all three of
these layers, being quite marked even in the muscular
coat; the adventitia, also, is considerably thicker than is
seen in arterial structures. The presence of these elastic
fibers doubtless explains the variation observed in the size
of the duct. When distended, it may be as large as 4 mm.
in diameter, while in its collapsed condition it is very
small and almost unrecognizable.

For the use of those who are interested in looking
up cases of anomalous distribution of the duct, a section
of anatomic references is given at the end of this
article.

*Physiology.*—Consideration of the physiology of the
lymphatic system is of very marked practical importance
from several standpoints. That the thoracic duct pos-
sesses a high degree of contractility would be strongly
suggested by its histologic structure, and has been
proved by theoretic and practical experimentation.
Boegehold mentions the observations of Dittrich, Ger-
lach, and Herz[14] on hanged criminals, where the elec-
trical contractility of the duct was observed as long as
36 minutes after death; and the observations of Henle
and Pfeuffer, in which contraction was observed 1½
hours post mortem. Experimentally with dogs, the
thoracic duct has been tied above, and after consider-
able pressure has accumulated by the filling of the recep-
taculum chyli, the duct has been incised longitudinally
between the receptaculum and the ligature; in several
instances the contractility was sufficient to close the
opening and preserve the integrity of the duct. It is of

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[14] Prager Vierteljahrsschrift, Feb. 3, 1851.

interest here to mention that the pressure in the thoracic duct during the interval of digestion is equal to from 9 to 15 mm. of mercury,[15] which is considerably more than the blood pressure in the jugular vein, 8 to 4 mm. of mercury, and less than that of the carotid artery, about 70 mm. of mercury (in rabbits).[16]

The physiologic aspect of complete occlusion of the thoracic duct, as observed in disease and animal experiments, are of importance with reference to the establishment of collateral circulation and rupture of the receptaculum chyli on the one hand, and the state of nutrition sustained by the organism on the other. The complete occlusion of the thoracic duct by disease without serious interference with the flow of chyle, has been observed. Such an instance, due to tuberculous thrombosis of the duct, is mentioned by Welch.[17] Other cases have been recorded. Occlusion of the duct, due to a pathologic process is, however, gradual to a greater or less extent, and the possibility of collateral circulation under such circumstances seems much greater than where the duct is suddenly occluded, as by ligature. A considerable amount of experimental work has been done on animals, mainly dogs and horses. This work was carefully reviewed by Boegehold, who collected the detailed results of these observations. He found that ligation of the duct resulted in complete obstruction of lymphatic circulation with rupture of the duct in but few instances, and that collateral circulation as a rule was rather readily established.

With reference to the degree of nutrition sustained after ligature of the duct, the experimental observations of Schmidt-Mulheim have been of marked importance. It was found that the absorption of albuminous material was practically unaffected, and that the nutrition of an animal could be maintained for a considerable time on such a diet. These experiments were performed on dogs on the supposition that the thoracic duct is always single in these animals, and that ligation of the duct in the neck prevented absolutely the entrance of chyle into the circulation. It has been since observed that the thoracic duct in the dog is subject to some variation, as in man, which deprives the experiment of a certain amount of value. It is a well-established physiologic fact, however, that the absorption of fat occurs almost entirely through the medium of the thoracic duct; that albuminous material is absorbed directly without entering the lymph flow of the thoracic duct, and that carbohydrates find their way through the duct only to a very limited degree, about 1 % of the total absorption. It

[15] Weiss, M., Virchow's Archiv, B. 22, S. 526.
[16] Foster, M., Text Book of Physiology, 1893, pt. 1, p. 205.
[17] Transactions of the Association of American Physicians, 1889, vol. 4, p. 76.

can, therefore, be stated with considerable confidence
that independently of the lymphatic circulation, a high
degree of nutrition can be sustained by the ingestion of
proteids and carbohydrates.

Several other physiologic facts may be mentioned
here, the pertinence of which will be indicated later.
With reference to the rapidity of the absorption of fat,
the observations of Erben in a case of chyluria are of
interest. He found that fat appeared in the urine within
2 or 3 hours after ingestion. Schäfer states that absorp-
tion of fat in a dog, after a full meal, continues for 30
hours. He also quotes Zawilski, who claims that the
amount of fat in the intestine during digestion is practi-
cally constant, and the rapidity with which it passes
from the stomach depends largely upon the rapidity with
which it is absorbed by the intestine. This view appears
to be generally accepted by physiologists. It seems rea-
sonable to conclude, therefore, that it would pass more
rapidly from the stomach following a period of starvation,
after fat absorption from the intestine had largely ceased.
But as it is known that fasting diminishes, to a certain
degree, the power to form normal digestive secretion, it
is probable that fat digestion would be slightly less rapid
after starvation. Harley, in speaking of normal absorp-
tion of milk fat, concludes from a number of experiments
performed on dogs that the maximum rate of absorption
is reached about 7 hours after taking food, after which
time it continues at about the same rate until completed,
regardess of the amount of fat introduced into the
stomach. With reference to the length of time liquid
or semi-liquid food remains in the stomach, Beaumont's
observations on Alexis St. Martin are extremely import-
ant, although it is not at all unlikely that the artificial
conditions existing in St. Martin altered somewhat the
peristaltic action of the stomach. He found that bread
and milk introduced through the gastric fistula was
completely passed from the stomach into the intestine by
the end of 3 hours. Absorption of fat would, of course, not
occur until after the material had entered the intestine.

The nature of lymph and chyle are of importance in
diagnosis. Foster, speaking of lymph, says, " Broadly
speaking, we may say that all the substances present in
blood plasma are present also in lymph, but are accom-
panied by a larger quantity of water." The presence of
fat in lymph forms the distinction between lymph and
chyle. The amount of fat in chyle in the thoracic duct
varies, about 5% being the common amount. In dogs it
has been found to vary from 2% to 15%. This increase
is due almost entirely to the presence of neutral fats. A
small part of the fat is present in fat globules of con-
siderable size, but the large proportion of it exist- in a
very minute stage of subdivision, resembling under the

microscope amorphous urates, and possessing "Brown-ian" movements. This minute subdivision of the fat constitutes what is commonly spoken of as the "molecular basis" of chyle. Lymph is almost colorless, resembling serum which one sees coming from wounds. Chyle resembles milk in appearance, and may or may not coagulate spontaneously. Spontaneous coagulation is due to the presence of fibrin, and when observed in wounds of the duct is probably due to the small amount of blood collected with the fluid, as chyle removed from an internal cavity, as in cases of chylous ascites, does not coagulate spontaneously. The most careful and exhaustive examinations of chyle that have been found recorded are mentioned by Whitla in an article on chylous ascites. This contains a careful investigation by himself of the fluid drawn from the abdomen in a case of this character, and a very extensive chemical examination by Hay, of Aberdeen; to these we would refer those wishing more extensive information. For clinical purposes, however, the presence of a milky fluid containing fat in minute subdivision is sufficient for making a diagnosis of chyle. The detailed references mentioned above may be found under *Physiology* at the end of the paper.

Having considered some theoretic and practical questions from an anatomic and physiologic standpoint, a more detailed study of the cases will be made. In 6 of the cases, Nos. 3, 6, 8, 13, 14, 17, injury of the duct or its branches was not suspected at the time of operation, while the remaining 11 cases, Nos. 1, 2, 4, 5, 7, 9, 10, 11, 12, 15, 16, it was known beyond reasonable doubt to have occurred. The subclavian and internal jugular veins were exposed, but uninjured in 7 cases, Nos. 2, 5, 7, 9, 13, 16, 17. Exposure of the veins was not mentioned in 4 cases, Nos. 1, 8, 12, 14, although in case No. 8 they were undoubtedly exposed. The subclavian was injured in 2 cases, Nos. 1, 3; the internal jugular vein in 2 cases, Nos. 4, 11. In the 2 cases of accidental injury, Nos. 10, 15, the question of injury to the large vessels could not be determined, though such an injury seems probable in case No. 15, where there was considerable hemorrhage. In 4 cases only, Nos. 5, 7, 9, 16, was the injury to the duct itself absolutely determined, and the anatomy of the parts satisfactorily developed. . In case No. 5 there was a longitudinal tear ¼ inch in a vessel ⅛ inch in diameter; the distance above the innominate vein was not mentioned. In case No. 7 the duct was wounded ½ inch above the innominate vein, size of opening not being given. In case No. 9 there was a longitudinal wound of 3 mm., 1 cm. above the subclavian vein. In case No. 16 the wound was 3 mm. long and 1 to 5 cm. above the clavicle. The height of the duct in the neck was determined in 3 cases: In cases Nos. 7, 9, it

was 4 cm. above its entrance into the vein, and in case
No. 16 it was 5 cm. above the sternum ; in the remain-
der the anatomic relations of the duct were not men-
tioned.

The discharge of lymph or chyle when it occurred at
the time of operation was slight in two cases, Nos. 10,
12, only moderate in five, Nos. 1, 2, 7, 9, 11, and was
quite profuse for a greater or less time in four cases,
Nos. 4, 5, 15, 16.   In two cases, Nos. 1, 16, the pressure
seems to have been considerable, in the latter the fluid
spurting up into the wound about 5 to 7 cm.   In these
cases the fluid appears to have been lymph only in six
instances, Nos. 1, 4, 5, 7, 9, 11, while chyle was dis-
charged at operation in the remaining five cases, Nos. 2,
10, 12, 15, 16 ; Nos. 10. 15, however, were accident cases
and not prepared for operation.   In case No. 1, although
the fluid appeared to have been lymph and the patient
had fasted for 12 hours, there was enough lymphatic
pressure to cause an appreciable degree of spurting, as
already mentioned ; in case No. 16, where the patient
had had breakfast 1½ hours before operation, chyle
spurted up 5 cm. to 7 cm.   In those instances where the
discharge did not appear until after operation, it became
evident the first day in case No. 3, the fourth day in
Nos. 13, 17, the fifth day in No. 14, and the tenth day
in Nos. 6, 8.  The nature of the fluid in these cases varied
of course with the period of digestion, and was undoubt-
edly lymph or chyle in each instance.   In the entire
series, however, the results of microscopic examination
of the fluid was mentioned in but three cases, Nos. 1, 5
and 17, and in the two latter fat was demonstrated in
very minute subdivision.   In No. 4 the fluid was said
to be "lymph," and in cases Nos. 6, 14 it was men-
tioned as "chyle," but the character was not given.   In
the remaining cases the diagnosis seems to have been
made on the gross appearance of the fluid, as no micro-
scopic or chemic tests were recorded.

The treatment of the 11 cases where the injury was
recognized at the time of operation was by packing,
suture and ligation.   Packing was employed in five
cases, Nos. 1, 2, 10, 11, 15, and another case, No. 4, was
undoubtedly also treated in this way, although the line
of treatment was not mentioned.  Lembert sutures were
employed in four cases, Nos. 5, 7, 9, 16, in the first three
fine silk being used, in the last fine catgut.   In case No.
9, the head and neck were encased in a plaster-of-paris
bandage to insure immobility.   Ligature was employed
in one case, No. 12, and was unsuccessfully attempted in
case No. 11, but the latter was finally packed.   The
cases that were packed, with one exception, No. 2, con-
tinued to discharge from the first dressing, but in No. 1
this discharge was very slight, scarcely staining the

dressings, and was of special interest, as the innominate and subclavian veins were both ligated. The patient lived for 36 hours, taking nourishment and stimulants. The flow of lymph, therefore, must have been through a collateral circulation or backward along the internal jugular vein, since it did not come out through the wound. The presence of valves, though imperfect, in the internal jugular vein about 1 inch above the innominate, renders the supposition somewhat stronger that the flow of lymph was accommodated by collateral circulation. In case No. 10 the leakage continued but a short time, while in No. 11, though slight, it persisted for three weeks. In Nos. 4, 15, the discharge was of large amount and was checked by secondary operation, as will be mentioned later. In the cases in which suture of the duct was employed, subsequent leakage occurred in two, Nos. 5, 7, but in each instance was thought to be due to wounded radicles, rather than to escape from the main duct. In No. 5 this discharge was profuse for five hours and considerable for the next 24 hours, after which it ceased entirely; in No. 7 the discharge continued for 15 days, though slight; in No. 9 the closure appears to have been perfect, the wound was closed without drainage, and no subsequent leakage occurred; this was the first case of suture without subsequent leakage, and the only case of suture in which the wound was closed successfully without drainage. In No. 16 there was no subsequent leakage, but a gauze drain which was introduced into the lower end of the wound was removed on the third day, healing taking place by first intention. The case in which ligation was employed, No. 12, showed no subsequent leakage; the method of closing the wound was not mentioned.

Packing was employed as a method of treatment in 5 cases, Nos. 3, 6, 8, 13, 17, in which the injury was not recognized until after operation. In No. 14 of this same series a graduated pressure pad was applied over the wound, and no mention was made of packing. In No. 3 packing appears to have been immediately successful, as there was no subsequent discharge. In cases Nos. 6, 8, 13 the wounds were packed but lightly, and profuse discharge continued. In No. 6 packing was abandoned, and subsequent operation performed, as will be mentioned later. Cases Nos. 8 and 13 were subsequently securely tamponed, and the discharge ceased immediately. In Nos. 14, 17 the discharge continued 14 and 18 days respectively; in the former case the employment of packing was not mentioned, in the latter secure packing was employed after a few days, but without very apparent effect. An interesting and instructive feature in all the cases in which packing was used is the fact that in those cases where light packing or drainage was em-

ployed there was subsequent discharge, whereas firm packing controled the discharge completely with the possible exception of one case, No. 17.

Subsequent or secondary operation was resorted to in 3 instances, Nos. 4, 6, 15. In case No. 4 the discharge was profuse and the constitutional effect was marked. The discharging point was successfully clamped, the clamp remaining on 3 days. In case No. 6, following light packing, there was abundant discharge, which soon caused marked general physical depression. A few days after the original operation, the wonnd was explored, the discharging vessel readily clamped, the clamp remaining on for 3 days. There was immediate improvement. In case No. 15, in which the injury was due to an accident, the wound was packed when first seen. The following day the wound was opened, the discharging point readily ligated and the wound completely closed. There was no further discharge.

Constitutional effect due to lymphatic discharge was evident in 3 cases, Nos. 4, 6, 8. In No. 4 the discharge was estimated at 3 pints daily, and the patient lost flesh rapidly; the vessel was subsequently clamped, and the patient gained flesh at the rate of a pound a day. In case No. 6 the discharge was estimated at $1\frac{1}{2}$ to 2 pints daily, and the constitutional effect was marked; the vessel was clamped, and immediate recovery occurred. In No. 8 there was profuse discharge for 8 days, during which time the patient lost 10 pounds; the wound was securely and successfully packed, and during the next 15 days the patient gained 23 pounds. In case No. 1 the patient died from "shock and exhaustion," and as there was no appreciable lymphatic discharge subsequent to operation, it seems unreasonable to attribute any constitutional effect to the injury of the duct. In No. 15 the patient was in a condition of exhaustion due to loss of blood. In No. 17, while there was considerable depression following the operation, the lymphatic discharge was so slight that it was not thought to bear any causal relation to the condition. In the remaining 11 cases no constitutional effect was observed, although in several there was slight discharge for a considerable time. When constitutional effect was noted, the rapidity with which it occurred, and the quickness and completeness of the recovery after the discharge had ceased, permitted no question as to the cause.

The prognosis of the series was very favorable, only one death occurring, No. 1, and that bearing no apparent relation to the injury of the duct. Gay, however, in reporting this case, ventures the opinion that the wound of the duct would have precluded the patient's recovery. One author, Schwimm, Case No. 6, speaks of injury of the thoracic duct as of "frightful importance."

Gerrish[18] remarks that "the prospects of success are not brilliant," and one writer[19] remarks that a wound of the thoracic duct is beyond surgical treatment. All others, however, who have ventured to express an opinion, are agreed that wounds of the thoracic duct are serious only to a very moderate degree, and it might be added that the most serious feature lies in the possibility of entirely occluding the duct by ligature, suture, or clamps.

Recommendations offered by writers for operative treatment are somewhat varied. The method of suture, among the more recent writers, is recommended first where possible, and is referred to by Kœnig and Keen and later by Cushing. Clamping the vessel and leaving the forceps on for several days, although practised in 2 cases, Nos. 4, 6, was recommended only in one instance; Schroeder and Plumber remark that clamping is Fenger's method of dealing with such injuries. Ligation has been recommended by Souchon[20], he having great faith in immediate collateral circulation. Cushing recommends, where suture is impossible, the placing about the duct of a provisional ligature which can be secured subsequently if packing is ineffectual and the failing condition of the patient justifies such a radical measure. He also recommends tying all visible lymphatics when working near the duct. Schwimm recommends ligating the lymph-vessels in the pedicle of the lower glands of the neck before they are entirely removed. An objection to all ligatures in the neighborhood of the duct is that the duct itself may be included, which as an immediate radical procedure does not seem justifiable at the present time. Keen stated this same objection, saying that ligatures should not be employed unless it was definitely ascertained that there were other ducts; this is, of course, scarcely applicable to ligating small lymphatic radicles as mentioned by Cushing. Placing a provisional ligature about the duct at the time of operation cannot be recommended, as ligation of the duct should not be performed until all other means, including a secondary operation, have been tried without avail. The ligating of lymphatic branches of any considerable size, or blindly ligating pedicles deep in a wound in the neighborhood of the duct does not appear justifiable, unless the duct has been developed by dissection, or unless the operator is sure he is not occluding the main channel. The same objection exists with reference to the use of clamps.

The value of packing is unquestioned, and mentioned by all. Study of the cases would certainly justify the

[18] Dennis' System of Surgery, 1895. vol. 2, p. 468.
[19] American Text Book of Surgery, 1888, p. 448.
[20] Park's Surgery, 1896, vol. 2, p. 255.

belief that accurate firm packing will control the discharge in all cases. In those instances in which the discharge was not controled by packing, it was said to have been lightly applied in several, and no mention was made of firm packing in the others. The objection that by packing, the lymphatic circulation may be entirely shut off, seems unreasonable, as the pressure of the lymphatic circulation would seem sufficient to preserve to a certain degree the integrity of the duct, especially as any packing is sure to become slightly loosened in the course of a few hours. One great value of packing, as mentioned by Cushing, is that it increases largely the chance for collateral circulation. The tampon is a safety valve allowing the escape of a certain amount of lymphatic fluid in case the lymph-pressure becomes too high before the new channels of circulation have been fully opened. It is not meant to be said that packing will control the entire discharge at once in every case, but that it will control it very largely at first, will do so completely after a short time, and will sometimes be effectual from the very beginning if properly used. The use by Warren of a graduated pad applied for pressure over the wound, is merely a less accurate method of reaching the same results. The employment by Cushing of a plaster-of-paris bandage, employed so extensively at the Johns Hopkins Hospital, seems an unnecessarily severe procedure. Absolute immobility cannot possibly be obtained, and it seems possible to secure a sufficient degree of support to the head by large cervical dressings carefully applied, and the use of sandbags in bed.

The theoretic explanations offered in those cases in which lymphatic discharge has not appeared until several days after operation, are not altogether satisfactory. It seems highly probable, in these instances, that only small radicles of the duct were injured, as discharge from a vessel of considerable size would probably have been recognized at the time of operation; whereas the escape of a small amount of clear fluid could readily be mistaken for serum. In two cases, however, the wound was subsequently investigated, and the exit of escape found to be of considerable size, in one instance being clamped, No. 6, and in another successfully packed, No. 8. It is noticeable also that the discharge in these 2 cases was delayed longer than in any others of the series, not appearing until 10 days after operation. The explanation offered by Schwimm and later by Cushing, that the discharge is due to increased lymph-pressure after feeding has been resumed, is not entirely satisfactory. The lymph-pressure in all the cases was probably at its height within a few days after operation, while in several instances the leakage did not appear to have commenced until several days after this period. In the

meanwhile the processes of repair must certainly have been going on. In the two instances in which the discharge was delayed for 10 days the above view seems justifiable, in spite of the possibility of there having been a very slight leakage during the entire period.

The question of subsequent enteric treatment, although of the utmost importance, appears to have received no careful or thoughtful consideration, and this is one point to which we would draw special attention. Gerrish[18] says "the patient is to be kept perfectly quiet, and be given such food as will barely save him from actual starvation, in the hope that by keeping the duct as nearly as possible empty the accidental opening will close." This is the most important suggestion found, but it lacks any specific recommendations. Agnew's suggestion,[19] that no food should be given in order to keep the walls of the duct collapsed, does not recommend itself ; a further suggestion in the same article, that milk may be introduced directly into the venous circulation, seems very properly to have never been attempted. Cushing recommends that the patient should receive a "meager diet," but says nothing further. From a physiologic standpoint, the indications for feeding in such cases seems very direct, namely, that nourishment should consist solely of proteids, with a possible addition of a small amount of carbohydrates, and that all fat should be avoided. That a sufficient degree of nutrition can be maintained on these materials has been demonstrated. The use of properly prepared beef juice and egg albumin from the white of an egg, meet the requirements in its most rigid aspect. Centrifugalized milk contains no fat, although it has considerable sugar. The slight absorption of carbohydrates through the lymph, however, does not make it a serious objection. Subsequently the use of oysters, fish, and raw vegetables may be satisfactorily employed. By such feeding the material passing through the thoracic duct can be reduced to a minimum, and at the same time the nutrition of the patient satisfactorily maintained. That the amount of lomph passing through the duct is somewhat increased by the ingestion of even albuminous fluids, is undoubtedly true. The amount of this increase, however, it has not been possible to ascertain from previous observations, and it is our future purpose to investigate this question by animal experiments.

One other very practical suggestion arises from a consideration of the physiology of digestion, and some of the experiments on which this suggestion is based were briefly enumerated at the end of the section on *physiology*. The appearance of lymph during the interval of digestion so closely resembles serum that its presence in a wound, unless in considerable amount,

would entirely escape detection. This undoubtedly has been the case in a number of instances where injuries of the duct or its branches were not suspected at the time of operation. The appearance of chyle, however, is so distinctive that its presence in a wound, even in small amount, would be almost sure to attract attention at once. Not only this, but the increased lymphatic pressure would surely open up and bring to notice slight injuries of the duct itself, or injuries to radicles which might very readily contract sufficiently to prevent the escape of lymph during operation, but would be opened up and discharge subsequently on the resumption of feeding. Low lymph-pressure and the absence of chyle are two of the most favorable conditions for overlooking a wound of the lymphatic system. No mention has been made of this point previously, so far as can be ascertained. The physiologic suggestion then, to induce the absorption of fat during operations in the neighborhood of the thoracic duct, seems eminently practical. The objection will be at once raised that distended lymphatics will be injured much more readily than those in a partially collapsed condition. The gross difference between partially filled and distended lymphatics would probably not be very noticeable owing to the small size of the vessels, and it seems probable that most, if not all of the wounds of the lymphatics, while distended, would occur if the vessels were only partially filled with lymph, the difference being that in one instance the wound would probably be apparent at the time, while in the other it might not be realized until after the operation, when high lymph-pressure was increased. The question of lymph-pressure must be met either at operation or soon after, and it seems preferable that this pressure should be exerted at the time when its effect can be observed and corrected immediately, if necessary, rather than later when its effect must be met blindly by inaccurate packing or secondary operation. Another objection which may be raised is that of introducing material into the stomach before giving an anesthetic. It must be remembered, however, that absorption of fat does not occur until the material reaches the intestine, after which its objection, from the standpoint of the anesthetist, does not exist. It would be desirable, however, to produce the effect by a material small in bulk and which will be passed out of the stomach readily and quickly. These requirements would seem to be most satisfactorily met by the use of a small quantity of cream, perhaps from 4 to 6 ounces. From experiments already mentioned, it is safe to assume that all, or nearly all, of this amount would be passed out of the stomach by the end of 8 hours if the patient had received previously an adequate enteric preparation for operation. The solid

material of cream being almost entirely fat, and in such a physical condition as to be most readily absorbed, so far as we know from physiologic experiments, the absorption of fat would probably begin within a short time, perhaps an hour, after the cream had entered the stomach. It has been shown that in animals the height of fat digestion is reached after about 7 hours, and that after a full meal it continues in dogs for nearly 30 hours. The previous enteric preparation for operation is mentioned in only 3 cases in the series. In cases Nos. 1, 5, the patients had fasted for 12 and 18 hours respectively and the discharge at operation was lymph and not chyle. As is customary, hevever, these patients had probably received a limited diet, largely albuminous, for some time previous. In case No. 16 the patient had been fed 1½ hours before operation, the pressure in the duct was considerable, and the fluid was chyle. It is to be regretted that the facts have not been recorded in more of the cases. The period of fat absorption being so prolonged, it seems certain that one would find chyle in the thoracic duct for at least a period of from 2 to 7 hours after the ingestion of cream on an empty stomach, and that if the material were given 3 hours before operation little if any cream would remain in the stomach as an objectionable feature from an anesthetic standpoint.

In conclusion, the following thoughts suggest themselves:

First.—The increasing frequency of extensive dissections in the neck makes it desirable to consider means of avoiding injury to the thoracic duct.

Second.—It is desirable that if wounds of the thoracic duct or its branches occur, they should be recognized at the time of operation. The result in Case A makes evident the advantage of such early recognition. As this case was operated upon after a meal, it suggests the ingestion of 4 to 6 ounces of cream 3 hours before operation. This might be especially desirable in secondary operations undertaken for the purpose of locating the point of injury. The desirability of such a procedure may be further studied by observations made upon animals.

Third.—That suture of the duct with fine silk or catgut be accomplished where possible; that all small discharging lymph radicles be ligated; that the ligating and clamping of lymphatic vessels of considerable size be avoided, unless the integrity of the thoracic duct itself has been demonstrated; that where suture of the duct or large radicles is impossible, gauze packing, firmly and accurately applied, be used; that the head and neck be kept at rest, the use of morphin to a considerable degree being recommended if necessary.

Fourth.—That until repair of the duct is thought to

be complete, nutrition should be sustained on albumin-
ous material, with possibly a small amount of carbo-
hydrates, but with an absolute exclusion of fats.

### REFERENCES.

#### Cases.

Allen, D. P., and Briggs, C. E. Present article. Operator, D. P.
Allen. Cases Nos. 16, 17.

Boegehold, E. Archiv für klinische Chirurgie, 1883, B. 29, S. 443.
Ueber die Verletzungen des Ductus thoracicus. Operator, Wilms.
Case No. 2.

Cushing, H. W. Annals of Surgery, 1898, Vol. 27, p. 719. Operative
Wounds of the Thoracic Duct. Report of a Case with Suture of the
Duct. Operators, C. A. Porter, W. S. Halsted, H. W. Cushing. Cases
Nos. 7, 8, 9.

Gay, G W. Boston Medical and Surgical Journal, 1875, Vol. 92, p.
422. Surgical Operations at the Boston City Hospital. Operator, D. W.
Cheever. Case No. 1.

Keen, W. W. The New York Medical Journal, 1891, Vol. 59, p. 569.
Operation Wounds of the Thoracic Duct in the Neck, with a Resumé
of Two Prior Recorded Cases and Two Additional Cases. Operators, A.
M. Phelps and W. W. Keen. Cases Nos. 4. 5.

Lund, F. B. Boston Medical and Surgical Journal, 1899, Vol. 140, p.
354 A Case of Operative Injury of the Thoracic Duct. Operators, F.
B. Lund and J. C. Warren. Cases Nos. 18, 14.

Lyne, W. H. Virginia Medical Semi-Monthly, 1898, Vol. 3, p. 278.
Stab Wound of the Thoracic Duct. Operator, W. H. Lyne. Case
No. 10.

Münter, A. Deutsche medicinische Wochenschrift, 1899, No. 48, p.
799. Schnittverlezung des Ductus thoracicus. Operator, A. Münter.
Case No. 15.

Schroeder, W. E., and Plumber, S. C. Annals of Surgery, 1898, Vol.
28, p. 229. Report of Two Cases of Injury of the Thoracic Duct in Oper-
ations on the Neck. Operators, W. E. Schroeder and S. C. Plumber.
Cases Nos. 11, 12.

Schwimm, J. Annals of Surgery. 1896, Vol. 23, p. 582. A Case of
Operative Injury of the Thoracic Duct at the Root of the Neck.
Operator, J. Schwimm. Case No. 6.

Vagedes, T. Inaugural Dissertation, Würzburg, 1885. Ueber Ver-
letzungen des Ductus Thoracicus. Operator, Maas. Case No. 3.

#### Anatomy.

Albin. Gesch. u. Beschr. des Saugadersystems. Mascagnis. B. 3,
S. 42.

Brinton, J. H. New York Medical Journal, 1891, Vol. 59, p. 568. The
Surgical Relations of the Thoracic Duct in the Neck, with Exhibitions
of two Dissections made by Mr. Ward Brinton.

Gray, H. Anatomy, Descriptive and Surgical, 1893, p. 682. The
Thoracic Duct.

v. Haller, A. Elementa Physiologie, T. 7, p. 222.

Henle. Anatomy, 1876, Vol. 3, p. 453.

Hyrtl. Lehrbuch der Anatomie. 12 Aufl., S. 956.

Klein, E. Elements of Histology. 1882, p. 90. The Lymphatic
Vessels.

Morris, H. Human Anatomy, 1893, p. 683. The Thoracic Duct

v. Patruban. Seltene Anatomische Beobachtungen. Oesterreich
Jahr. 6, Juli, 1844.

Piersol, G. A. Normal Histology, 1898, p. 117. The Lymphatic
System.

Schäfer, E. A. Quain's Anatomy, Vol. 1, pt. 2, p. 378. Lymphatic
System.

Stöhr, P. Lehrbuch der Histologie, 1892, p. 82. Lymphgefässys-
tem.

Svitzer. Müller's Archiv, 1845.

Thane, G. D. Quain's Anatomy, 1892, Vol. 2, pt. 2. p. 517. The
Thoracic Duct.

Watson, Journal of Anatomy, 1872, Vol. 10, p. 427.

Wutzer. Müller's Archiv, Heft 4, 1834.

#### Physiology.

Beaumont, W. The Physiology of Digestion, 1847, p. 153.

Colin. Traité de Physiologie comparée des Animaux. Paris, 1823.
T. II

Cooper, A. Medical Records and Researches. London, 1798.

Three Instances of Obstruction of the Thoracic Duct, with Some Experiments Showing the Effects of Tying that Vessel.

Dittrich, Gerlach, Herz. Präger Vierteljahrsschrift, February 3, 1851.

Flandrin. Handwörterbuch der Physiologie, Nasse. B. 1, S. 246.

Foster, M. Textbook of Physiology, 1891, pt 2, p. 496. The Nature and Movement of Lymph (including Chyle).

Harley, V. Journal of Physiology, 1895, Vol. 18, p. 1. The Normal Absorption of Fat, and the Effect of Extirpation of the Pancreas on it.

Henle and Pfeuffer. Zeitschrift, 1852, B. 2.

Leuret and Lassaigne. Recherches Physiologiques et Chimiques, pour servir à l'Histoire de la Digestion. Paris, 1825, 8, p. 178.

Magendie and Dupuytren. Journal de Physiologie, T. 1, p. 21.

Schäfer, E. A. Textbook of Physiology, Vol. 1, p. 463.

Schmidt-Mulheim. Archiv für Physiologie, von du Bois-Reymond, 1877, S. 553.

Weiss, M. Virchow's Archiv, B. xxii, S. 525.

Welch, W. H. Transactions of the Association of American Physicians. 1889, Vol. 4, p. 56.

Whitla, W. British Medical Journal, 1885, Vol. 1, p. 1069, "Chylous Ascites."

### Miscellaneous.

American Textbook of Surgery, 1898, p. 448. Rupture of the Thoracic Duct.

Dennis, F. S. System of Surgery, Dennis, 1895, Vol. 3, p. 220. Injuries of the Thoracic Duct.

Dennis, F. S. Surgery by American Authors, Park, 1896, Vol. 2, p. 270. Injuries of the Thoracic Duct.

Gerrish, F. H. System of Surgery, Dennis, 1895, Vol. 2, p. 468. Wounds of Lymphatic Vessels.

Hamilton, J. B. International Textbook of Surgery, Warren-Gould, 1900, Vol. 1, p. 918. Rupture of the Thoracic Duct.

Kirschner. Archiv für klinische Chirurgie, 1885, B. 32, S. 156. Ein Fall von rechtseitigen Chylothorax in Folge von Ruptur des Ductus thoracicus nebst Statistik und Kritik der bisher bekannten einschlägigen Fälle.

Koenig, F. Lehrbuch der Speciellen Chirurgie, 1898, B. 1, S. 553. Verletzung des Ductus thoracicus.

Murray, J. International Textbook of Surgery. Warren-Gould, 1900, Vol. 2, p. 204. Injury of the Thoracic Duct.

Souchon, E. Surgery by American Authors, Park, 1896, Vol. 2, p. 255. Wounds of the Lymphatic Duct.

# LAPAROTOMY FOR PERFORATION IN TYPHOID FEVER.[1]

## REPORT OF SIX CASES.

### By C. E. BRIGGS, A.M., M.D.,

#### OF CLEVELAND, OHIO.

*(From the Surgical Clinic of Dr. Dudley P. Allen, Lakeside Hospital.)*

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THE report is based upon the six cases of laparotomy for intestinal perforation during the course of typhoid fever, occurring in Lakeside Hospital since its opening in January, 1898. These were performed in 1899 and 1900 during the writer's service as resident surgeon, and, with the exception of the last case, came under his immediate observation and care. The inclusion of this last case in the series is perhaps of doubtful propriety, since the patient entered the hospital as a case of general peritonitis and was treated as such, the case containing very little of interest with reference to the surgical treatment of typhoid perforation. For the purpose of completeness, however, it has been added.

It is due to the courtesy of the visiting staffs of Lakeside Hospital that the present report has been made possible, and to these gentlemen the writer wishes to acknowledge his obligation.

CASE I.—Male, aged forty-seven years. Moderately severe case. At entrance, leucocytes 5700 per cubic millimetre. Widal reaction negative, diazo positive. Bowels rather loose, no hemorrhage. Symptoms of perforation on the twenty-first day of the disease ; abdominal pain, sensitiveness, rigidity, and moderate distention. Rise in pulse and temperature; slight vomiting ; leucocytes 4460 per cubic millimetre. Condition unfavorable.

*Operation.* Five hours after appearance of symptoms. Chloroform. Time, thirty minutes. Right lateral incision. Dark-brown abdominal fluid. Perforation of ileum 8 centimetres from cæcum ; closed with continuous Lembert catgut sutures. No threatening perforation found. Irrigation with sterile water ; intestines not removed. Gauze drainage. Cultures from abdominal fluid, bacillus coli communis. Death seventy-five hours after operation, apparently from exhaustion.

*Autopsy,* restricted. Local peritonitis about lesion and gauze packing, catgut sutures absorbed, and perforation patent. Four other neighboring perforations opening into the same area of local peritonitis. Confluent ulcers of cæcum, not perforating. No general peritonitis. Cultures from local peritonitis, bacillus coli communis; from general peritoneal cavity, negative.

C. K., medical No. 769 ; surgical, No. 909. Service of Dr. H. H. Powell. Male, aged forty-seven years, white, German, married, carpenter. Admitted August 5, 1899 ; discharged August 15th. Dead.

*Family History.* Negative.

*Previous History.* Had always been well, strong, and active. Twelve years ago he had malarial fever; six years ago he had what was taken to be typhoid fever, being ill for nine weeks; no other illnesses recalled; habits good; no venereal history.

*Present Illness.* Patient entered hospital complaining of headache, loss of appetite, diarrhœa, and fever. Headache was the first symptom, beginning two weeks previous to entrance, and persisting. There was also anorexia and diarrhœa, the latter being quite troublesome. There was some abdominal pain in the region of the umbilicus.

*Physical Examination.* Patient well-nourished and developed; mind clear; face flushed; tongue coated. Pulse 80, good quality. Temperature 101.8.° Lungs negative. Heart not enlarged; soft systolic murmur at apex. Spleen enlarged on percussion, not palpable. Abdomen soft, slightly sensitive about umbilicus; numerous rose-spots. Leucocytes 5700 per cubic millimetre. Urine, no albumin; faint diazo reaction. Widal reaction negative.

During the next six days the symptoms were those of a moderately severe case of typhoid, the temperature running 101° to 103°, during which time he had six tub baths, four of which were given in the last two days. The bowels remained rather loose. The urine continued to show a diazo reaction, and there was a slight trace of albumin. No subsequent Widal tests were made.

On August 12th, the twenty-first day of the disease, the patient began to have abdominal pain, coming on rather gradually and being first noticed at 6.30 A.M. At first it was confined to the lower half of the abdomen, gradually spreading upward and becoming general. Pain was also noticed at end of penis. He vomited a slight amount of curdled milk at 8 A.M. The temperature at 6 A.M. was 101°, and at 9 A.M. had risen to 102.2°, and the pulse had risen from 72 to 104 during the same period. The leucocytes at 9 A.M. were 4460 per cubic millimetre, and this unfortunately was the only count made. At 9.30 A.M. the patient was seen with Dr. W. H. Nevison. The abdomen was moderately distended and tympanitic. There was marked sensitiveness over the entire lower half of the abdomen, and the abdominal wall was generally quite rigid. Respirations 28, largely costal. Pulse was 124, dicrotic, readily compressible. The lungs were clear, the heart as previously described. The general condition of the patient was poor, although not altogether unfavorable for operation.

*Operation,* August 12th, 10.30 A.M., by Dr. W. H. Nevison, five hours after first appearance of symptoms. Anæsthetic, chloroform, preceded by morph. sulph., gr. one-quarter, hypodermically. Time, thirty minutes.

Light anæsthesia. Incision eight centimetres long in right linea semi-lunaris opposite anterior superior spine. Considerable dark-brown fluid escaped, fecal odor, containing small particles of extraneous matter thought to be feces. Cæcum readily found and ileum carefully inspected for about one hundred and twenty centimetres. A perforation was found about eight centimetres from the cæcum. It was round, about three millimetres in diameter, on the free side of the bowel, and from it fecal matter was escaping. The area of induration surrounding this opening was about two centimetres in diameter. No other perforations were found in the explored ileum or cæcum, nor were any perceptibly

thinned areas appreciable, although careful search was made.    The
perforation was turned in without excision by a double row of con-
tinuous Lembert catgut sutures.    The ileum was dark and congested,
the cæcum somewhat so.    Other coils of intestine seen were slightly
congested.    Appendix normal.    Parietal peritoneum seemed but slightly
congested.    Presence of enlarged glands not observed.    No fibrinous
flakes seen.    There were no adhesions.    Abdominal cavity thoroughly
irrigated with a large quantity of sterile water, special attention being
paid to the pelvis and the lumbar fossæ.    The intestines were not
handled, but the irrigation was thoroughly accomplished by means of
a hard-rubber flushing tube.    Site of suture left near the surface, and
to it iodoform gauze drainage was placed, brought out through the
lower end of the wound.    Above this the wound was closed with inter-
rupted silkworm-gut sutures through all layers.    During the operation
the patient received strych. sulph., gr. one-fifteenth, hypodermically,
and an infusion of seven hundred cubic centimetres of normal salt solu-
tion.    The radial pulse was very rapid and weak, imperceptible at
times.    The operation was associated with considerable shock, the
patient being in a poor condition on leaving the table.

The subsequent treatment of the case was by strychnine, nutrient
stimulating enemata, liquids without milk by mouth, subcutaneous
infusions of salt solution, sponge baths, and oxygen.    Patient took
nourishment well during entire time.    He was slightly delirious and
semi-conscious at times, but for the most part his mind was clear and
active.    There was slight abdominal distention, but practically no pain
except on the day following the operation, when it was quite marked
in the lower half of the abdomen for a short time.    The discharge from
the abdomen was very profuse during the last twenty-four hours, and
was dark colored, which, together with the pain mentioned above,
suggested strongly a second perforation in the locality of the gauze
drainage.

The temperature remained about 102.5° to 104° rectal, and the
pulse 120 to 130.    On August 15th, three days after the operation, the
patient began to show evident signs of dissolution, the pulse-rate
increased steadily, and the quality became progressively worse.    There
was some general abdominal distention, most marked in the epigastrium.
There was an accumulation of coarse, moist râles throughout the chest,
and the respirations were labored.    Oxygen was given during the last
seven hours.    He was unconscious for six hours before death.    He died
August 15th, at 3.05 P.M., seventy-five hours after operation.

The bacteriological examination of the abdominal fluid at the time
of the operation showed on cover-slip preparations a medium-sized
bacillus and a small coccus, singly and in pairs.    Plate cultures showed
a pure growth of bacillus coli communis.    No growth of the coccus
mentioned could be found.

*Autopsy.*    This unfortunately was restricted.    About the gauze pack-
ing and the site of the lesion in the ileum there was a localized peri-
tonitis, as was to be expected.    Opening into this localized area was
the original ulcer.    The catgut suture had been almost entirely absorbed.
There were four small neighboring perforations of the ileum, which
also opened into this same localized area.    There were several confluent
ulcers of the cæcum which had not perforated.    There was no general
peritonitis.    Cultures taken from the area of local peritonitis showed

bacillus coli communis.    Cultures and cover-slip preparations from general peritoneal cavity were negative.

CASE II.—Male, aged seventeen years; severe case.  At entrance, leucocytes 5980 per cubic millimetre; Widal reaction negative; diazo reaction negative.  Marked constipation; slight distention.  Hemorrhage on seventeenth and eighteenth days of disease, preceded by considerable abdominal pain.  Symptoms of perforation on eighteenth day of disease; abdominal pain, sensitiveness, rigidity, moderate distention, rise in pulse, temperature unaffected, slight vomiting.  Condition very unfavorable.

*Operation.*  Eight hours after appearance of symptoms.  Chloroform.  Time, twenty-five minutes.  Right lateral incision.  Dark-brown abdominal fluid with curds.  Perforation of ileum twenty-five centimetres from cæcum; one threatening perforation close by; both secured with continuous Lembert silk sutures.  Irrigation with salt solution and sterile water; intestines not removed.  Gauze drainage.  Cultures from abdominal fluid, bacillus coli communis.  Death sixteen hours after operation; general peritonitis.

*Autopsy,* restricted.  Intestinal suture intact.  No other perforations found.  General peritonitis.  Cultures from general peritoneal cavity, bacillus coli communis.

J. B., medical, No. 779; surgical, No. 925.  Service of Dr. J. H. Lowman.  Male, aged seventeen years, white, American, single, student.  Admitted August 13, 1899; discharged August 22d.  Dead.

*Family History.*  One brother died of typhoid fever; one sister ill with typhoid fever at present time.

*Previous History.*  Children's diseases.  Always strong and active; habits good; no venereal history.

*Present Illness.*  Patient entered hospital complaining of headache, constipation, and general malaise.  Headache was the first symptom, and was first noted ten days previously.  Bowels constipated, no movement for forty-eight hours before entrance.  No hemorrhages.  Chilly sensation during last two nights; no distinct rigor.  Epistaxis on day of entrance.

*Physical Examination.*  Patient well nourished and developed; athletic.  Face flushed; tongue slightly coated, trembles when protruded.  Pulse 116, low tension, dicrotic.  Temperature 102.8°.  Lungs negative.  Heart slightly enlarged to the left, loud systolic murmur at apex.  Spleen slightly enlarged on percussion, not palpable.  Abdomen rather tense, not tympanitic, no especial sensitiveness, no rose-spots recorded.  Leucocytes 5980 per cubic millimetre.  Urine, no albumin, no diazo reaction.  Widal reaction negative.

During the next four days the symptoms were those of a severe typhoid.  The nervous symptoms were marked.  There was a little abdominal pain on two occasions following tub baths.  Baths were given every three hours with but few intermissions.  Reactions following baths were not very good.  The pulse ranged from 90 to 120, and was of rather low tension.  On one day patient complained of considerable pain on inside of right leg, extending down to the knee.

On August 18th, at 8 P.M., following tub bath, there was sudden sharp pain in lower half of abdomen, which continued for some little time, but with rather less severity.  The temperature was unaffected, but the pulse-rate was increased somewhat.  Sponge baths were sub-

stituted. No blood examination was made. During the next day there was slight abdominal pain with an occasional increase in severity. The abdomen was somewhat distended, but this passed off after several free bowel movements. Following this the pain practically disappeared, and the patient was comfortable. There was no vomiting. Pain was present along inner side of right thigh. Leucocytes were 8000 per cubic millimetre in the morning, and 10,000 per cubic millimetre in the afternoon. The next day, August 20th, the abdominal pain had practically disappeared, but there was slight sensitiveness above the pubes and in the left inguinal region. Tub baths were resumed, and were borne rather better than previously. A small amount of old clotted blood was passed in one of the stools.

August 21st, the eighteenth day of the disease, the patient had been rather more comfortable than usual. At 2 A.M., while in tub bath, there was sudden severe pain in the lower abdomen. The abdomen was tense, not distended, and quite generally sensitive. The temperature was unaffected. The pulse rose from 80 to 110, and was not well sustained. At 2.45 A.M. the patient passed about two drachms of blood in a bowel movement. The patient vomited curdled milk at 3 A.M. Abdominal pain continued; sensitiveness was quite marked, more so in the right lower quadrant. Sponge baths were substituted. No blood examination was recorded. At 9 A.M. the patient was seen with Dr. W. H. Nevison. His general appearance was that of a very sick and much reduced man. The finger nails and lips were slightly cyanotic. Pulse was 120, regular, small volume, low tension. Respirations were 24, thoracic. The abdomen showed moderate general distention and tympanites. There was general sensitiveness, slightly more marked in the lower half, and marked muscular resistance. The condition of the patient seemed quite unfavorable for operation.

*Operation*, August 21st, 9.45 A.M., by Dr. W. H. Nevison, eight hours after perforation was thought to have occurred. Anæsthetic, chloroform, preceded by morph. sulph., gr. one-quarter, hypodermically. Time, twenty-five minutes.

Light anæsthesia. Incision in right linea semilunaris nine centimetres long, at level of anterior superior spine. A moderate amount of dark fluid containing particles of curdled milk escaped. Cæcum readily found, and ileum searched for about one metre from cæcum. About twenty-five centimetres from cæcum a perforation was found on the free margin of the gut, three millimetres in diameter; base generally thickened. About six centimetres from this thickened area a very thin centre was made out. Nothing more approaching perforation was found. Perforation was turned in without excision by two rows of running fine silk Lembert sutures for a distance of about two and five-tenths centimetres. The thin ulcer was also turned in with a single running silk suture. About the perforation was a little gray fibrinous deposit. The ileum had lost its gloss in places, but in general looked well. No fibrinous exudate outside the region of perforation. The cæcum and appendix normal. Remaining coils of intestines and parietal peritoneum appeared to be in good condition. No adhesions were found. Abdomen flushed with hot salt solution and sterile water in large quantities, special attention being paid to the dependent portions. This was done by means of a hard-rubber flushing tube. The intestines were not removed from the abdominal cavity. The site of

suture left near wound, and to it was placed iodoform gauze drainage, brought out through lower end of wound, above which the incision was closed with interrupted silkworm-gut sutures through all layers.   During operation patient's pulse became very feeble, respiration shallow, color poor.   He was given strych. sulph., gr. one-fifteenth, hypodermically, divided, and a saline infusion of eight hundred cubic centimetres, under which the condition improved somewhat.

The subsequent treatment was by strychnine, nutrient stimulating enemata, subcutaneous infusions, and sponge baths.   The reaction to the sponging was very marked, and the baths were given with considerable care.   The patient's condition improved slightly for a few hours following the operation, after which time he failed steadily, and died August 22d, at 2 A.M., sixteen hours after the operation.

Bacteriological examination of the free abdominal fluid at operation showed a pure growth of bacillus coli communis on plate cultures.   No cover-slip preparations were made.

*Autopsy.*   This was very restricted.   The intestinal suture was intact. No further perforation was found.   There was a general peritonitis with thin turbid fluid.   Cultures from the general peritoneal cavity showed bacillus coli communis ; no cover-slip preparations were made.

CASE III.—Male, aged thirty-one years ; mild case with a moderately severe relapse.   At entrance leucocytes, 5700 per cubic millimetre ; Widal reaction positive ; diazo reaction negative.   Bowels rather constipated ; no hemorrhages.   Symptoms of perforation on forty-third day of disease, twelfth day of relapse ; severe abdominal pain, general sensitiveness, moderate distention, marked muscular rigidity on right side ; rise in pulse, temperature unaffected ; slight vomiting ; leucocytes, 31,600 per cubic millimetre.   Condition of shock, but fairly favorable for operation.

*Operation.*   One hour after symptoms.   Cocaine solution, 1 per cent. Time, twenty-five minutes.   Right lateral incision.   Little brownish abdominal fluid.   Perforation of ileum forty-five centimetres from cæcum, closed with double continuous Lembert silk suture ; no threatening perforations found.   Irrigation with sterile water, intestines not removed.   Gauze and glass-tube drainage.   Cultures from abdominal fluid showed staphylococcus pyogenes aureus.   Death fifty-eight hours after operation ; typhoidal toxæmia.

*Autopsy,* restricted.   Sutures intact ; no other perforation ; no general peritonitis ; no peritoneal adhesions except around drainage.   Cultures from general peritoneal cavity, negative.

T. D., medical No. 992 ; surgical No. 1304½.   Service of Dr. E. F. Cushing.   Male, aged thirty-one years, white, Welsh, married, coachman.   Admitted January 25, 1900 ; discharged February 28th.   Dead.

*Family History.*   Negative.

*Previous History.*   Always strong and active, no definite diseases recalled ; habits good ; no venereal history.

*Present Illness.*   Patient entered hospital complaining of headache, weakness, and lack of energy.   Symptoms began ten days before entrance, with malaise.   Following this there was severe headache, anorexia, slight cough, and marked weakness.   He also had several attacks of abdominal pain described as " colic."   The bowels were loose, but there had been no hemorrhages.   Patient had vomited several times.   There was no epistaxis.

*Physical Examination.* Well nourished and developed. Mind clear; tongue coated. Pulse 100, full, not dicrotic. Temperature 102°. Lungs and heart negative. Spleen enlarged on percussion, not palpable. Abdomen slightly distended and slightly sensitive on pressure; covered with scattering rose-spots. Leucocytes 5700 per cubic millimetre; hæmoglobin, 90 per cent. Urine, no albumin, no diazo reaction. Widal reaction positive.

For the next three weeks the patient ran a course of mild typhoid fever without complications; the temperature rarely rose above 102.5°, and for a large portion of the time was below 102°. The patient suffered no abdominal pain, and there were no intestinal hemorrhages.

On February 14th, the thirty-first day of the disease, the temperature began to rise, and the patient suffered a well-marked relapse. During the next twelve days the symptoms were somewhat more aggravated than during the primary attack; the temperature ran somewhat higher, though at no time was extreme; on several occasions there was nausea and a limited degree of vomiting. There was no abdominal pain, the abdomen was soft, not distended. Urine contained a faint trace of albumin; diazo reaction positive. Patient was somewhat constipated; there were no intestinal hemorrhages.

On February 26th, the forty-third day of the disease and the twelfth day of the relapse, the patient was given an enema at 9 A.M., which was but slightly effectual. Following this he complained of feeling a little distended, and there was slight abdominal pain. This pain, however, soon passed off, and at 10 A.M. the patient was found sleeping quietly; pulse 100. When seen fifteen minutes later he was in a condition of evident shock; he was cyanotic and trembling; the pulse had reached 120, and was very compressible; temperature unaffected. There was quite severe general abdominal pain, the abdomen was somewhat distended, but not very sensitive. The liver appeared to be pushed upward. The patient vomited once, about an ounce of greenish fluid. Leucocytes 31,600 per cubic millimetre. The patient was seen with Dr. D. P. Allen at 10.30 A.M. Cyanosis was still present. Pulse was 130, low tension. Respirations were 30, thoracic. The abdomen was moderately distended; there was general, not localized, sensitiveness, and there was marked muscular rigidity on the left side; peristalsis was present. The heart sounds were weak, the lungs clear. Patient's condition was fairly favorable for operation.

*Operation,* February 26th, 11 A.M., by Dr. D. P. Allen, one hour after appearance of symptoms. Local anæsthesia, cocaine solution, 1 per cent., preceded by morph. sulph., gr. one-quarter, hypodermically. Time, twenty-five minutes.

Incision six centimetres long in right linea semilunaris opposite anterior superior spine, carried into peritoneal cavity without causing the patient pain. Abdominal cavity contained a little brownish fluid. Cæcum readily found, normal. Appendix normal. Perforation of ileum about forty-five centimetres from cæcum, on free border, about two millimetres in diameter. Perforation closed without excision by two rows of continuous silk Lembert sutures. No other perforations or threatening perforations found, but the ileum was not examined beyond the lesion. Abdomen irrigated with large quantities of hot sterile water with flush tube, intestines not being removed; special attention was given to the lumbar fossæ and pelvic cavity. Ileum con-

siderably congested. Peritoneal surfaces otherwise apparently unaffected. No fibrinous flakes. No adhesions seen. Glass-tube and gauze drainage placed to seat of suture, on either side of which the wound was closed with interrupted silkworm-gut sutures. The patient's condition did not appear to be affected by the operation; the pulse was as good as before operation. Very little pain was experienced except during irrigation, when it was moderate.

Subsequent treatment of the case was by strychnine, nutrient and stimulating enemata, subcutaneous saline infusions, sponge baths, and liquids by mouth. The patient appeared to be unaffected by the operation. During the next two days the course was that of an increasingly severe typhoidal toxic condition with the accompanying evidence of exhaustion during the second day. There was failing pulse, marked trembling, moderate delirium at times. The abdomen was only slightly distended, was generally tympanitic, and was but moderately sensitive. At times there was sharp abdominal pain. There was but little discharge from the wound. Urine showed a large trace of albumin, and contained an abundance of hyaline and granular casts. The patient died at 9.10 P.M., February 28th, fifty-eight hours after operation.

Bacteriological examination of the free abdominal fluid at the time of operation showed on cover-slips a few cocci and numerous bacilli. Tube cultures showed a pure growth of staphylococcus pyogenes aureus.

*Autopsy*, restricted. The intestinal sutures were intact, the perforation being firmly closed. No additional perforations found. There was no general peritonitis. There were no peritoneal adhesions except those about the gauze packing. Cultures and cover-slip preparations from general peritoneal cavity were negative.

CASE IV.—Female, aged sixteen years; very severe case. At entrance leucocytes 9932 per cubic millimetre; Widal reaction positive; diazo reaction positive. Bowels moved readily with enema, no hemorrhages. Marked delirium. Symptoms of perforation on the fifth day of the disease; abdominal pain, rigidity, distention; rise in pulse and temperature; no vomiting; leucocytes 15,080 per cubic millimetre; general constitutional change marked. Exploration advised.

*Operation.* About four hours after first appearance of symptoms. Cocaine solution ½ per cent. Time, twenty minutes. Short right lateral incision. No perforation; peritoneal cavity apparently normal. Wound sealed with collodion dressing. Cover-slips and cultures from abdomen negative. Medical treatment uninterrupted by operation. Subsequent course of fever severe; convalescence slow.

H. B., medical No. 1035. Service of Dr. H. S. Upson. Female, aged sixteen years, colored, American, single, cleaner. Admitted January 4, 1900; discharged March 24th. Cured.

*Family History.* Negative.

*Previous History.* Children's disease; no other illness recalled; habits good.

*Present Illness.* Patient was transferred from gynecological service complaining of general weakness. Two days before patient complained of general malaise and ached all over. There had been a little cough, occasional epistaxis, anorexia, and vomiting with moderate frequency. Bowels regular.

*Physical Examination.* Patient well nourished and developed; mind clear; tongue coated. Pulse 100, fair strength and volume, slightly

dicrotic. Temperature, 104.2°. Lungs and heart negative. No enlargement of spleen perceptible. Abdomen soft, no rose-spots. Leucocytes, 9932 per cubic millimetre; hæmoglobin, 85 per cent. Urine, albumin faint trace; diazo reaction present. Widal reaction positive.

From the start the symptoms were those of a very severe typhoidal infection. The temperature was high, averaging 104° to 105°. The reaction from the tub baths was not satisfactory, and the drops in temperature very moderate. The pulse for the first three days averaged 110 to 120, but was of fair quality. There were marked nervous symptoms, the patient being delirious most of the time and rarely giving an intelligent answer to questions. The amount of stimulation required was considerable.

On January 6th the patient complained somewhat of abdominal pain, and there was slight distention but no rigidity. On January 7th, the fifth day of the disease, the patient's condition began to get markedly worse in the early part of the evening. The patient was delirious, so that her subjective sensations were of little avail in diagnosis. In spite of the delirium, however, she complained of abdominal pain, which it seemed must be at least moderately severe to arrest her attention at all. The abdomen was moderately distended, and was everywhere tympanitic. There was a considerable degree of muscular rigidity. No definite sensitiveness could be localized. The pulse had risen from 120 to 140, was weak and dicrotic. The temperature had risen from 102.8° at 5 p.m. to 105.5° at 8 p.m. The leucocytes at 8 p.m. were 15,080. The patient was seen about 8 p.m. with Dr. G. W. Moorehouse, and essentially the same condition found as noted above. A definite diagnosis of perforation could not be made. The constitutional effect, however, from some cause or other had been very marked, and owing to the delirious condition of the patient and apparent insensibility to ordinary degrees of pain it was felt that a perforation under the circumstances would be very easily overlooked, and that the physical condition was such as one might readily expect in a patient so severely ill if a perforation had actually occurred. On account, therefore, of the possibility of overlooking a perforation, together with the degree of abdominal symptoms afforded by the patient in even such a delirious condition, an exploration under local anæsthesia was advised. The risk of such an operation was very slight, whereas the danger from an unrecognized perforation was of the gravest possible character.

*Operation*, January 7th, 9.45 p.m., by Dr. C. E. Briggs, about four hours after the appearance of symptoms. Local anæsthesia, cocaine solution, ½ per cent., preceded by morph. sulph., gr. one-quarter, hypodermically. Time, twenty minutes.

Incision three centimetres long in right linea semilunaris opposite anterior superior spine. On opening the peritoneum no free fluid was found. There was no injection of the cæcum or adjoining portions of the ileum. No adhesions were found, and the peritoneal cavity appeared to be perfectly normal. Cover-slip preparations from right iliac fossa and pelvis showed no organisms. Wound closed with buried silk sutures in layers. A collodion dressing was applied, consisting of several alternate thin layers of sheet wadding and collodion, making a firm and absolutely impervious dressing. Condition of patient apparently unaffected by operation. Permission given to continue baths within four hours if desirable. Patient remained on the medical service.

The subsequent history of the case is of little interest from the present stand-point, except for one attack of abdominal pain. She ran the course of a very severe typhoidal infection, the toxic symptoms being so severe on several occasions that her recovery seemed hopeless. The temperature remained persistently high for nearly ten days, and was but slightly affected by tub baths. On only one occasion, January 20th, the eighteenth day of the disease, was there any subsequent suggestion of an abdominal complication. On this day she was awakened at 2 A.M. by severe abdominal pain. The pulse was but slightly affected. The temperature was unchanged. The abdomen was soft and not sensitive, and there was very slight sensitiveness on deep pressure in right lower quadrant. The pain could not be definitely localized, although the patient was perfectly rational, and it passed off within a short time. The leucocytes, however, at 2.30 A.M. had risen to 50,660 per cubic millimetre; two days before the leucocytes were 8060, and five days later 9600 per cubic millimetre. The convalescence was slow and uneventful. Following the operation, baths were given as required without reference to the incision. The incision healed by first intention. The patient was discharged March 24th, cured.

*Bacteriological Examination.* Cultures taken from the right iliac fossa and pelvis showed no organisms in cover-slip preparations, and there was no growth on cultures.

CASE V.—Male, aged seventeen years; mild case. At entrance leucocytes 4900 per cubic millimetre; Widal reaction positive; diazo reaction positive. Bowels rather constipated, no hemorrhages. Symptoms of perforation on twentieth day of disease; severe abdominal pain, general sensitiveness, slight distention, marked muscular rigidity in lower half of right side; rise in pulse; fall in temperature of 1°; no vomiting; leucocytes 9200, 13,000, 13,200 per cubic millimetre. Condition of patient favorable for operation.

*Operation.* Three hours after first appearance of symptoms. Cocaine solution, 1 per cent.; chloroform. Time, fifty-five minutes—forty minutes under chloroform. Right lateral incision. Yellowish-gray abdominal fluid. Perforation eleven centimetres from cæcum, closed with continuous Lembert silk sutures; no threatening perforations found. Irrigation with sterile water. Intestines not removed. Glass-tube drainage from pelvis. Cultures showed bacillus mucosus capsulatus. Recovery.

C. W., medical No. 1208; surgical No. 1530. Service of Dr. E. F. Cushing. Male, aged seventeen years, white, American, single, laborer. Admitted June 16, 1900; discharged August 19th. Cured.

*Family History.* Negative.

*Previous History.* Has always been well and strong. A few years ago had erysipelas, and later a fever the nature of which he did not know. Habits good; no venereal history.

*Present Illness.* Patient entered hospital complaining of headache, backache, and pain in stomach. Two weeks previously symptoms began with general aching sensation and tired feeling. Shortly after this he began to have nausea, and there was anorexia. Epistaxis was frequent. Bowels rather costive. Had been in bed one week.

*Physical Examination.* Fairly well nourished and developed; mind clear; face flushed; lips dry; tongue coated. Pulse 80, full, but readily compressible, dicrotic. Temperature 101.8°. Lungs and heart

negative. Spleen apparently not enlarged. Abdomen not distended, soft, and showing numerous rose-spots. Leucocytes 4900 per cubic millimetre; hæmoglobin, 85 per cent. Urine, albumin faint trace; diazo reaction present. Widal reaction positive.

During the next five days the symptoms were those of a rather mild case of typhoid fever, the temperature coming down gradually, with good drops following tub baths. There was no diarrhœa, no intestinal hemorrhages. The abdomen was soft and flat. The progress of the case was very satisfactory.

On June 22d, the twentieth day of the disease, the patient had been as usual all through the day. No tub baths had been given. At 6.30 P.M. he was seized with a sharp abdominal pain which was not definitely localized. When seen a few minutes after this there was no abdominal distention, but marked muscular rigidity and general sensitiveness. The pulse was 76 and of good quality; the temperature 102.8°, which was 1° higher than at 4 P.M. The leucocytes at 6.45 P.M. were 9200 per cubic millimetre. The pain was sufficient to make the patient groan audibly. A small enema with turpentine, two drachms, was given, which was followed by a light-yellow stool and a small amount of gas, but afforded no relief from the pain. Morph. sulph., gr. one-quarter, was given hypodermically. At 7 P.M. the pulse was 88, and the temperature had fallen 1°. At 7.30 P.M. the patient was seen with Dr. J. L. Martin. The pulse was 110, low tension, readily compressible. The patient had a dusky appearance, and there was marked cyanosis of the lips and finger-nails. Respirations were shallow, mostly thoracic. The abdomen was not distended, but there was marked rigidity over the lower half, and was a little more evident on the right side; there was considerable general sensitiveness. The patient still complained of moderately severe pain in lower half of abdomen. At 8 P.M. the pulse had risen to 120. The cyanosis was slightly less marked, but otherwise the condition was about the same. The leucocytes were 13,000 per cubic millimetre. At 8.30 P.M. the leucocytes were 13,200 per cubic millimetre.

*Operation*, June 22d, 9.30 P.M., by Dr. C. E. Briggs, three hours after first appearance of symptoms. Local anæsthesia, cocaine solution, 1 per cent., preceded by morph. sulph., gr. one-quarter, hypodermically; chloroform. Time, fifty-five minutes, forty minutes of which were under chloroform.

On reaching the operating-table the abdominal pain was still present, and there was slight distention. The cyanosis was considerably less. Pulse 120. Under local anæsthesia an incision was made six centimetres long in right linea semilunaris. Although the patient suffered no pain, he became very nervous and quite beyond control, and light chloroform anæsthesia was substituted. Owing to the boy's nervous condition the opening of the abdomen under cocaine required great patience, consuming fifteen minutes. On opening the peritoneum a moderate amount of thin, yellowish-gray fluid escaped. Cæcum readily found, ileum reached, and perforation found on its free border about eleven centimetres from the ileocæcal valve. It was about two millimetres in diameter and exuded bowel contents when pressed. About it the bowel was red and thickened for about two centimetres in diameter. The perforation was wiped off with bichloride and turned in with two rows of running fine silk Lembert sutures for a length of three centi-

metres. Over these were placed three interrupted Lembert sutures to relieve the strain, as the bowel was very friable. The cæcum and ileum for about one metre were searched with eye and finger for perforations or thin ulcers, but nothing suggesting a threatening perforation was found. The ileum for about half this distance was injected and seemed somewhat thickened. Appendix normal. No fibrinous flakes were observed. No adhesions were found. Incision enlarged to nine centimetres. Abdomen was thoroughly irrigated with a large amount of sterile water, with special reference to the pelvis and flanks ; the intestines were not removed. The pelvis contained a large amount of thin, purulent-looking material, rather different in appearance from that seen on opening the abdomen. Examination of cover-slip preparations from this fluid showed numerous large and small bacilli and a few small cocci. Intestinal coils near pelvis were injected, but remainder of abdomen appeared nearly normal. Abdomen flushed till perfectly clear. Glass drainage-tube placed in pelvis, brought out through lower end of wound, above which the wound was closed with interrupted silkworm-gut sutures. The site of perforation was left immediately below the incision. During the operation the patient's pulse remained at 120, good quality, rising a little during recovery from anæsthesia. Patient was but very slightly under chloroform, and was moving most of the time except during closure of the abdominal wall. The forty minutes under chloroform were largely spent in careful examination of the bowel, and in very thorough irrigation of the peritoneal cavity.

The subsequent treatment of the case was by nutrient and stimulating enemata, strychnine, sponge baths, and liquids by mouth. During the first night there was very profuse sweating, which was relieved by atropine. The day after the operation, June 23d, the patient began to vomit a dark-brown fluid, and this continued for several hours, the patient's general condition becoming considerably affected. The stomach was washed out, about three pints of dark-greenish fluid being evacuated, after which the vomiting ceased, and there was immediate and steady improvement.

From this time on the patient made a progressive and uninterrupted recovery, the pulse coming down to between 80 and 90 on the second day after the operation, and the temperature falling gradually to 99° by the end of the first week. The leucocytes on the second, sixth, and eighth days after operation were 15,400, 5400, 5600 per cubic millimetre, respectively. The discharge from the wound was moderate. The glass tube was gradually withdrawn, being replaced by gauze packing on the eighth day, which was entirely omitted four days later. The wound was very indolent, and there was considerable sloughing, but no active suppuration. The wound was entirely healed four weeks after operation, but owing to the persistence of a slight degree of fever —99° to 99.5°—the patient was kept in bed nearly two weeks longer. The cause of this temperature was never discovered. The patient was discharged August 19th, fifty-eight days after operation, in excellent condition.

*Bacteriological Examination.* Cover-slips and cultures taken from the abdominal fluid when the peritoneum was first opened were negative. Cover-slips taken from the seat of the ulcer and from the turbid pelvic fluid mentioned showed medium-sized bacilli and a few small cocci. Plate cultures from these two localities showed bacillus mucosus

capsulatus. Cultures taken from the bottom of the drainage-tube four days after operation gave a pure growth of the same organism.

CASE VI.—Male, aged twenty-eight years. Patient entered hospital with general peritonitis; no history obtainable. At entrance leucocytes 10,600 per cubic millimetre; Widal reaction positive; diazo reaction positive. Diarrhœa followed by constipation; no intestinal hemorrhages. Marked abdominal distention, rigidity, pain, and sensitiveness. Date of perforative symptoms not determined.

*Operation.* Period after perforation not known. Ether. Time, thirty minutes. Right lateral incision. Turbid abdominal fluid. Perforation of ileum thirty centimetres from cæcum; closed by continuous Lembert catgut sutures. Irrigation with sterile water; intestines not removed. Gauze and glass-tube drainage. Cultures from abdominal fluid, unidentified bacillus, probably bacillus coli communis, or bacillus mucosus capsulatus. Death four hours after operation, general peritonitis.

*Autopsy.* Intestinal sutures intact, no other perforations. General peritonitis. Cultures from heart, lungs, kidneys, and brain, bacillus mucosus capsulatus; from general peritoneal cavity, negative.

J. K., medical No. 1302; surgical No. 1660. Service of Dr. E. F. Cushing. Male, aged twenty-eight years, white, German, single, laborer. Admitted August 20, 1900; discharged August 21st. Dead.

History was obtained subsequently for purposes of record, but no information was at hand at time of entrance for aid in diagnosis.

*Family History.* Negative.

*Previous History.* No former illnesses known. Habits good.

*Present Illness.* Patient entered hospital complaining of abdominal pain. The symptoms began with headache eight days previously. For the last six days he had abdominal pain with some distention. There was diarrhœa at first, but during the last few days there was but one movement. There was no vomiting or epistaxis. No fever was noted. Was in bed only part of this time. Abdominal pain had been constant.

*Physical Examination.* Patient entered in the evening, and no history was available to aid in diagnosis. Moderately well developed, poorly nourished. He had the appearance of a very sick man. Tongue coated and dry. Pulse 120, irregular, but moderately strong. Temperature 100.8°. Lungs: on right side below clavicle there was slightly increased vocal fremitus; otherwise negative. Heart appeared not enlarged, sounds weak. Liver dulness from fourth to sixth rib in mammary line. Spleen: dulness anterior to about mid-axillary line; palpation impossible on account of distention. Abdomen distended, tympanitic, moderately rigid, sensitive to pressure, more marked in lower half and possibly slightly increased on right side; no rose-spots; doubtful dulness in both flanks. Leucocytes 10,600 per cubic millimetre at 9 P.M. Urine: albumin ⅓ per cent.; diazo reaction faint. Widal reaction positive; both of these examinations made the following morning.

The case was thought to be one of general peritonitis from perforation of a typhoid ulcer, although the existence of typhoid fever was not absolutely determined until the next morning. Circumstances, however, made an immediate operation impossible. During the night he was very actively stimulated. The next morning the Widal reaction determined the diagnosis. The case was seen by Dr. D. P. Allen about

9 A.M. The abdominal distention was extreme. There was general tympany, marked muscular rigidity, and general sensitiveness. The patient was in a condition of profound shock. Pulse 140 and very poor quality ; temperature 105.6° ; respirations 40. The case was considered practically hopeless.

*Operation*, August 21st, 10.30 A.M., by Dr. D. P. Allen. Time, after onset of symptoms not known. Anæsthetic, ether. Time, thirty minutes. Incision seven centimetres long in right linea semilunaris opposite anterior superior spine. On opening the peritoneum a moderate quantity of straw-colored fluid and thin pus escaped, containing fecal matter. Perforation of the ileum was found on the free border about two millimetres. in diameter, about thirty centimetres from the cæcum. This was closed with two rows of running catgut sutures, strengthened by four interrupted silk sutures. There was considerable agglutination of the intestinal coils in the neighborhood of the perforation, together with congestion of the remaining coils of intestines and the parietal peritoneum. No other perforations found. A considerable amount of thin pus was found high up under the liver and a considerable amount in the pelvis. The abdomen was thoroughly irrigated with sterile water, the intestines not being removed. Gauze and glass-tube drainage from pelvic cavity and subhepatic region. Pulse during the operation 180, very weak, often imperceptible. The patient was highly stimulated with strychnine and subcutaneous saline infusions. There was no reaction, however, and he died at 3 P.M., four hours after the operation.

*Bacteriological Examination.* Cover-slips from the abdominal fluid showed cocci and small bacilli. Tube cultures showed a pure culture of bacillus coli communis or bacillus mucosus capsulatus, the exact identity apparently not having been established.

*Autopsy,* complete, No. 194, August 26th. Anatomical diagnosis, typhoid fever, ulceration, and perforation with general peritonitis ; apical tuberculosis and hypostatic pneumonia ; acute splenic tumor. Special lesion ; thirty centimetres above cæcum there was a perforating ulcer of the ileum, closed with catgut sutures, which were still intact ; there were several other ulcers with very thin bases in the neighborhood, but no perforations. Cultures from heart, lungs, kidneys, and brain showed bacillus mucosus capsulatus ; from general peritoneal cavity, negative, owing probably to the recent irrigation.

GENERAL CONSIDERATIONS. That all six cases were typhoid fever is readily established. The Widal reaction was positive in four cases —III., IV., V., and VI. In the first two cases of the series the Widal reaction was negative at entrance, and for some reason was not recorded later. The course of the disease was perfectly typical in all instances. A perforation was found in all cases except Case IV., and this case had a positive Widal reaction. Autopsy in the fatal cases—I., II., III., and VI.—showed typical bowel lesions.

The cases with one exception—Case V.—were all severe infections, and this severity, not the complication, was held responsible for the death in two cases—I. and III. One case—III.—occurred during a moderately severe relapse, following a rather mild primary course.

The bowels were constipated in three cases—II., III., and V.—in the first of which the condition was very marked. In one case—Case I.—there was moderate diarrhœa. In Case IV. the bowels moved easily with enema, neither marked constipation nor diarrhœa being observed. In Case VI. the bowels were loose at first, followed by rather aggravated constipation.

Intestinal hemorrhages occurred in only one instance—Case II. In this case it was present on the seventeenth and eighteenth days of the disease, was slight in amount, but was accompanied with considerable abdominal pain. The last hemorrhage was apparently coincident with the perforation.

The ages were sixteen, seventeen, seventeen, twenty-eight, thirty-one, and forty-seven. There was but one female in the series—Case IV. She was colored, and no perforation was found. The remaining cases were males, and white. In Finney's series but one case occurred in a negro, and that was fatal.

SIGNS AND SYMPTOMS. As compared with the large proportion of the more extended collections, the cases presented show a remarkably distinct set of symptoms. In Case VI. the patient entered with unmistakable signs of general peritonitis, and the primary symptoms of perforation in this case were not observed. The discussion of the signs and symptoms is restricted, therefore, to the first five cases.

The date of appearance of symptoms was the fifth day in Case IV. ; the eighteenth day in Case II. ; the twentieth day in Case V. ; the twenty-first day in Case I. ; the forty-third day, the twelfth day of a relapse, in Case III. In Case VI., judging from the probably inaccurate history, the perforation occurred early, probably on the fifth or sixth day.

The abdominal symptoms were quite well marked in all cases. Pain appeared suddenly in three cases— Cases II., III., and V., and came on gradually in two cases—Cases I. and IV. It was confined to the lower half of the abdomen in three cases—Cases I., II., and V., but in Case I. it eventually radiated to the upper half and became general. In Case III. it was general, and in Case IV. it appeared to be general, but the delirious condition of the patient made accurate observation impossible. The pain was severe in three cases—Cases II., III., and V.—and moderate in two cases—Cases I. and IV. In Case I. pain also radiated to the penis, which was the only instance. Sensitiveness to pressure was slight in two cases—Cases II. and IV. ; moderate in Case III. ; marked in Cases I. and V. It was general in three cases—Cases III., IV., and V., and was confined to the lower half of the abdomen in two cases—Cases I. and II. Increased sensitiveness in the right lower quadrant so frequently spoken of was not observed.

Muscular resistance was a very marked sign in all but one of the

cases—Case IV. In this instance the resistance was but moderate, and no perforation was found. The resistance was general in three cases—Cases I., II., and IV., and was confined to the right half of the abdomen in one case—Case III. In Case V. it was confined to the lower half of the abdomen, and was considerably more marked on the right side. Distention was observed as moderate in Cases I., II., III., and IV., but was present to a slight degree only in Case V. Tympany to a greater or less extent was observed in all of the cases. Slight vomiting was observed in Cases I., II., and III., and was absent in Cases IV. and V.

The pulse showed a marked rise in all instances—20 to 50 beats. The quality of the pulse also became progressively worse with the increase in the number of beats, and was a very valuable sign. In Case IV., where no perforation was found, the pulse rose very gradually from 120 to 140. The marked severity of the case, however, made all of the signs and symptoms in this instance particularly difficult to estimate with much accuracy. The temperature was unaffected in two cases—Cases II. and III.—and in two cases—Cases I. and IV.—there was a distinct rise, 101° to 102.2°, and 102.8° to 105.5°, respectively. In but one case—Case V.—was there a fall in temperature, and in this instance of but 1° only, 102.8° to 101.8°. The respiratory rate was markedly increased. The nature of the respirations, however, was noted as largely thoracic in all the cases. This was especially marked, together with a very shallow quality, in Case V.

The condition of general systemic shock, as observed shortly before operation, was very marked in Case II., and was present to a considerable degree in Case IV. It was noted as moderate in Cases I., III., and V. Cyanosis, especially of the lips and finger-nails, was marked in Case V., moderate in Case III., slight in Cases I. and II., and absent in Case IV.

The white blood count as recorded showed a distinct rise in all but one instance—Case I. The records are as follows: Case I., entrance, 5700 per cubic millimetre; perforation, six days later, 4460 per cubic millimetre. Case II., entrance, 5980; perforation, eight days later, no count recorded. Case III., entrance, 5700; perforation, thirty-two days later, 31,600. Case IV., entrance, 9932; symptoms of perforation, two days later, 15,080. Case V., entrance, 4900; perforation, five days later, 9200, 13,000, 13,200. Case VI., entrance, 10,600. It is to be noted in Case IV. that subsequent to the operation the leucocytes on one occasion rose from 8060 to 50,660, associated with considerable abdominal pain, but no other constitutional effect.

THE CONDITION OF PATIENT AT OPERATION. The cases with but one exception—Case V.—were rather unfavorable to operation, two ʼng quite so, and one practically hopeless. As this is regarded as of lerable importance, the conditions will be given in more detail:

Case I. The patient's condition was poor, although not absolutely unfavorable to operation. The perforation occurred on the twenty-first day of the disease, in a moderately severe case, before the patient had begun to recover at all from the effects of his illness. He was weak and emaciated, and had comparatively little recuperative power. Case II. This case was quite unfavorable for operation. The patient was a strong, athletic boy, but the case had run a severe course, and the perforation occurred on the eighteenth day during the very height of the disease. The patient was weak and exhausted, and the rapidity with which he succumbed to the peritoneal infection was not surprising. Case III. This case was somewhat more favorable, although not very promising. The perforation occurred during the height of a rather severe relapse, being the forty-third day of the disease, the twelfth day of the relapse. He was quite weak, but appeared at the time to have a fair degree of strength. Case IV. The case was desperately sick at the time perforation was feared, but the symptoms appeared so early, the fifth day, that the patient's constitution had not been badly reduced. On this account it is believed she would have stood fairly well a more extensive operation. Case V. The condition of this patient was very favorable for operation, in marked contrast to the other cases. The case was mild, and when the perforation occurred, the twentieth day, the temperature had begun to come down ; he was not badly reduced. Case VI. The case, as stated, was *in extremis* at entrance, and was regarded as practically hopeless.

DURATION OF SYMPTOMS. The lapse of time between the first appearance of symptoms and the operation was short in all but one instance—Case II. In Case III. the operation was performed one hour after the appearance of symptoms. Cases V., IV., and I. were operated upon within three, four, and five hours, respectively, although the exact time of suspected perforation in Case IV. was somewhat indefinite, owing to the delirium of the patient. Case II. was opened eight hours after definite symptoms first appeared ; three days previously the patient had had abdominal pain following a tub bath, which grew less the next day, disappeared entirely the day before active symptoms, and was entirely unassociated with constitutional signs suggesting perforation. The duration of symptoms in Case VI. could be only roughly estimated, as perforation occurred before entrance, but it was probably twenty-four to forty-eight hours.

OPERATION. The technique of the operations presented very little that was distinctive. The anæsthetic was general in four cases, local in two cases. Chloroform, very lightly given and preceded by morph. sulph., · gr. one-quarter, was administered in Cases I., II., and V. Ether was similarly given in Case VI. Local anæsthesia, cocaine solution, ½ and 1 per cent., preceded by morph. sulph., gr. one-quarter, was employed

in Cases III. and IV. In Case V. the abdomen was entered under cocaine, but the nervous condition of the patient required the administration of chloroform.

The incision in each instance was in the right linea semilunaris opposite the anterior superior spine, three to nine centimetres long. In each instance, except Case IV., the cæcum was readily found, the ileum, cæcum, and appendix examined. In Case IV. the peritoneal cavity was so visibly normal that the ileum was not withdrawn. This, however, was considered a fault in the operation. An examination of the ileum was made for about one metre in Cases I., II., and V., but in Cases III. and VI. the inspection was not carried beyond the perforation. In all cases careful search was made for thin areas, threatening perforations, as well as for complete perforations. The perforation was excised in no instance. The closure of the perforation was by two rows of continuous Lembert sutures in each case, in two of which—Cases V. and VI.—these were strengthened by another line of interrupted silk sutures. The suture material was catgut in Cases I. and VI., and silk in the remainder. The irrigation was with very large quantities of sterile water, by means of a large flushing tube. With this tube all parts of the peritoneal cavity were readily reached, special attention being given to the lumbar fossæ and pelvic cavity. Only the portion of the ileum examined was removed from the abdomen, and an effort was made to handle the intestines as little as possible. Drainage was used in all cases except the exploration—Case IV. Iodoform gauze alone was used in Cases I. and II.; glass-tube and iodoform gauze in Cases III. and VI., and a single glass drainage tube from the pelvis in Case V. The site of the suture was left close to the abdominal wall in all instances. The wounds were all partially closed with interrupted silkworm-gut sutures through all layers, except Case IV., which was completely closed with interrupted buried silk sutures. The time of operation was twenty minutes in one case, twenty-five minutes in two cases, and thirty minutes in two cases. In Case V. fifty-five minutes were consumed, fifteen minutes in going through the abdominal wall under cocaine, and forty minutes, or the remainder of the operation, under chloroform. The condition of the patient was apparently unaffected by the operation in Cases III. and IV.; it was excellent in Case V.; was poor in Cases I. and II., and very bad in Case VI.

PATHOLOGY. Pathological observations of the cases are of special interest, and it is to be greatly regretted that more complete autopsies could not be obtained.

There was a moderate degree of peritonitis at the time of operation in all the cases of perforation, judging from the amount of free fluid in the abdominal cavity. In Case I. there was considerable dark-brown fluid with fecal odor; in Case II. a moderate amount of dark fluid; in

Case III. a small amount of brownish fluid; in Case V. a moderate amount of thin, yellowish-gray fluid, and in the pelvis a large amount of thin, purulent-looking fluid; in Case VI. a moderate amount of straw-colored fluid with a large accumulation of thin, purulent fluid under the liver and in the pelvis.

The perforation was single in each instance, and occurred on the free border of the ileum. In only one case—Case II.—was a threatening perforation found. The perforations were all small, two to three millimetres in diameter, and were surrounded by an indurated friable base about two centimetres in diameter in several instances. In one case—Case II.—there was a small amount of fibrinous exudate in the neighborhood of the perforation. The perforations were eight, eleven, twenty-five, thirty, and forty-five centimetres from the cæcum in Cases I., V., II., VI., and III., respectively.

The ileum, aside from the perforation, was altered in each instance, ranging from slight congestion to a thickened dark appearance. The appendix was normal in all cases. The cæcum was appreciably congested in Case I. only. The remaining coils of intestines were slightly congested in Case I. In Case V. those lying in the pelvis were considerably congested; in Case VI. there was a marked congestion, and agglutination of the coils in some places. The parietal peritoneum was appreciably congested in Cases I. and VI. only. In none of the cases were there fibrinous flakes in the peritoneal cavity, except for a small amount of deposit about the perforation in Case II. No adhesions were observed in any of the cases except in Case VI. In Case IV., in which the symptoms appeared on the fifth day and no perforation was found, the abdominal cavity was perfectly normal so far as could be observed.

*Bacteriology.* Bacteriological examination of the free abdominal fluid was made in all cases, but in only one instance was a culture taken from the perforation. Cover-slip preparations from Case I. showed a medium-sized bacillus and a small coccus; plate cultures grew bacillus coli communis only. Case II. showed a pure growth of bacillus coli communis in plate cultures. Case III. showed in cover-slips a few cocci and numerous bacilli; in plate cultures, a pure growth of staphylococcus pyogenes aureus. Case IV., in which no perforation was found, cover-slips and cultures were negative. Case V., cover-slips and cultures from fluid on first opening the abdomen were negative; cover-slip preparations from the perforation and the turbid pelvic fluid showed numerous medium-sized bacilli and a few cocci. A plate culture from these two localities gave a pure growth of bacillus mucosus capsulatus; a tube culture taken from the bottom of the drainage-tube in the pelvis four days after operation showed a pure culture of the same organism. In Case VI. cover-slip preparations showed cocci and small bacilli, the

nature of which was not definitely determined, but was apparently
bacillus coli communis or bacillus mucosus capsulatus.

*Autopsies,* complete, Case VI., or restricted, Cases I., II., and III.,
were made in the four cases of death. General peritonitis was present
in two cases only—Cases II. and VI.—in the other two cases the gen-
eral peritoneal cavity being free from fluid and adhesions, and the cul-
tures from the same being negative. Case I., death seventy-five hours
after operation, showed a local peritonitis about the gauze packing,
into which the original perforation and four small neighboring perfora-
tions opened ; the catgut sutures were almost entirely absorbed ; no
general peritonitis : the ileum showed several large confluent ulcers,
not perforating. Cultures from the local peritonitis showed bacillus
coli communis ; cover-slips and cultures from general peritoneal cavity
were negative. Case II., death sixteen hours after operation, sutures
intact, no other perforations ; general peritonitis, cultures growing
bacillus coli communis. Case III., death fifty-eight hours after opera-
tion ; intestinal sutures intact, no additional perforation ; no general
peritonitis, cover-slips and cultures from general peritoneal cavity nega-
tive. Case VI., death four hours after operation ; suture intact, no
other perforations : general peritonitis ; cultures from heart, lungs, kid-
neys, and brain showed bacillus mucosus capsulatus ; cultures from gene-
ral peritoneal cavity were negative, probably owing to recent irrigation.

RESULTS. In considering the results of these cases from the stand-
point of operations for the relief of typhoid perforation, it is manifestly
improper to include Case VI., which was suffering from general peri-
tonitis before the case was seen at all, and was operated upon solely for
the relief of the abdominal infection. Case IV., in which no perfora-
tion was found, adds one other to the increasing list of explorations
without untoward results in cases of suspected perforation, but cannot,
of course, be included in the list of cases where perforation has actually
occurred. In the four remaining cases with perforation, one alone
recovered, Case V. In all four cases there was a sufficient degree
of peritonitis to cause an accumulation to a greater or less degree of
free abdominal fluid, in which organisms were found in both cover-
slip preparations and cultures. Only one case—Case II.—as shown at
autopsy, died of general peritonitis. In this instance the operation was
deferred eight hours, the longest delay in the series, and an evident
mistake. The other two fatal cases—Cases I. and III.—showed local
peritonitis about the packing, as occurs in any abdominal wound that
is drained, but the general peritoneal cavity was free from fluid and
adhesions, and no organisms were obtained from it in cover-slip
preparations or cultures. It can be safely said, then, that whatever
else one may wish to consider the cause of death in these two cases, it
was not general peritonitis. A very large percentage of the fatal

cases following operation so far reported, at least 80 per cent., died from general peritonitis. The percentage cannot be given with any great degree of accuracy, however, owing to the small number of post-mortem examinations. The fact that it was possible to prevent the occurrence of general peritonitis in three out of four cases of perforation is worthy of note despite the fact that only one case recovered. The two fatal cases without general peritonitis—Cases I. and III.—lived seventy-six and fifty-eight hours, respectively, after operation. In Case III. the perforation occurred at the height of a moderately severe relapse, in which the clinical evidence of increasing typhoidal toxæmia was apparent before operation. The operation was performed under local anæsthesia without shock to the patient that was apparent to careful observation. It is confidently believed that this death was due to typhoidal toxæmia, and was independent of the operation. As a complete autopsy was not obtainable, however, this statement cannot be maintained with absolute certainty, although it is very strongly supported by clinical symptoms and the absence of general peritonitis. In Case I. perforation occurred on the twenty-first day during the height of the fever in a moderately severe case, before the patient had begun to recover from the effects of the disease, and it was evident that he had very little recuperative power. The clinical appearance of the patient on the last day of life was one of exhaustion and gradual heart failure, and was not unexpected, owing to the condition of low vitality which was apparent before operation. This of course was added to very materially by the shock of operation, which was, unfortunately it is believed in this instance, performed under general rather than local anæsthesia. It was also undoubtedly added to in a considerable degree by four subsequent perforations near the original lesion. The closure of the perforation was not successful, owing to the subsequent absorption of the catgut sutures. By rare good fortune the four subsequent perforations had opened along the line of drainage, and the extravasation was being cared for completely, as far as could be seen at autopsy, by the gauze drainage going down to the original perforation. The general peritoneal cavity was entirely free from evidences of peritonitis, there being no fluid or adhesions, and the cover-slip preparations and cultures from the same being negative. It is believed that the patient died of exhaustion. It is certain he did not die of general peritonitis. Here, again, however, the absence of complete autopsy leaves the absolute cause of death somewhat in doubt.

*II*

## INTESTINAL PERFORATION DURING THE COURSE OF TYPHOID FEVER, AND ITS SURGICAL ASPECTS.

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Frequency and Mortality of Perforation. While the percentage of deaths resulting from typhoid fever, and more particularly the proportion of these deaths due to perforation of the bowel is a well-established fact and quite generally known, we believe that the specific appreciation of the appalling number of these individual cases of perforation is by no means appreciated by the medical profession in general. While we all appreciate that the death rate from typhoid fever is from 7 to 14 per cent., averaging, probably, for the entire United States about 10 per cent., and that of these fully one-third are due to perforation, we think that few could have read without marked surprise the statistics recently collected by Dr. H. M. Taylor in an article on "Typhoid Perforation: Its Frequency, Prognosis, Diagnosis, and Treatment," *New York Medical Journal*, February 1, 1902, vol. lxxv. p. 193. From various statistical sources gathered in 1896 the author has determined the number of cases of typhoid fever in the United States as about 500,000 per annum, and the death rate about 50,000, which is doubtless a very fair average mortality. The frequency of perforation has been so definitely established from so many sources as being about 33⅓ per cent. of the deaths, that this number can hardly be questioned. This would give a death rate of something over 16,660 cases from perforation in typhoid fever in one year in the United States. Of this number it is now definitely known that 5000 to 8000 cases annually can be saved by operative interference. These figures represent, we believe, an adequate appreciation of the usefulness of surgical interference in the United States at the present time, and are certainly striking and instructive.

Owing to the very rapid medical and surgical progress along the lines of diagnosis and treatment in typhoid perforation during the last five years, the usefulness of operation in such cases has become established so far beyond the possibility of any doubt that it is no longer found necessary to urge and justify the procedure in the large majority of the cases. The question of recovery in such cases without operation

is a matter of very grave doubt, although it has been absolutely known
to occur in a few isolated instances where the damage was well local-
ized near the cæcum, the cases assuming more the characteristics of
appendicitis than those of perforation.  It is an unwarrantable assump-
tion, however, that unoperated cases recovering from mild or even
marked symptoms of perforation are actual cases of recovery from per-
foration itself.  At a time when medical treatment was practically the
only means employed, the possibility of recovery was a very serious
question even among the best authorities.  In an article by Dr. R. H.
Fitz (*Transactions of the Association of American Physicians*, 1891, vol.
vi. p. 200) on "Intestinal Perforation in Typhoid Fever: Its Prog-
nosis and Treatment," the author states:  "Since perforation of the
intestine in typhoid fever may take place without any subjective
symptoms, and since suggestive—even so-called characteristic—symp-
toms may occur without any perforation having taken place, it must
be admitted that recovery from such symptoms is no satisfactory evi-
dence of recovery from perforation."  Any practitioner who has been
intimately associated with typhoid fever for any length of time has
seen cases of typhoid suggesting perforation that have gone on to re-
covery, but too often there has been an unwarranted assumption that
perforation actually occurred, and the instance has been mentioned as
a remarkable cure.  Since the usefulness of operation has been estab-
lished in these cases it has become a well-known fact that the gravest
symptoms of perforation may be present without the actual lesion,
and, on the other hand, a rather premature assumption from vague
symptoms has been absolutely justified by the discovery of perforation
at operation.  It is needless to say that these remarks apply to the
diagnosis of perforation and not to the diagnosis of general peritonitis
following perforation.  The same position, however, the lack of signs
and symptoms corresponding to the actual pathological condition, has
been long since established with reference to general peritonitis that
has recently been demonstrated with reference to typhoid perforation.
The man who assumes an unassailable position in either one of the
above-mentioned conditions in instances which cannot be subjected to
actual demonstration, can no longer be considered to hold a tenable
and justifiable position.  It must be admitted at the present time that
it is a far safer and much more justifiable assumption that the mor-
tality in unoperated cases of intestinal perforation in typhoid fever is
practically 100 per cent.

  It was eighteen years ago that the first operation for perforation
was performed.  Dr. W. W. Keen, in 1898, in his book on *Surgical
Complications and Sequelæ of Typhoid Fever*, published a table of 83
cases collected by Dr. T. S. Westcott, and in the *Journal of the Ameri-
can Medical Association* for January 20, 1900, in an article on "The

Surgical Treatment of Perforation of the Bowel in Typhoid Fever,"
the same author gives a table of 75 additional cases collected by Dr.
M. B. Tinker, 158 cases in all, which were considered to include all
the cases published to January 1, 1900.  Since that time the number of
published cases has rapidly increased, but owing to greater familiarity
with the subject and the increased frequency of operation it is believed
that the number of published cases is far below the number of opera-
tions performed, especially in unsuccessful cases.  The majority of
the reports have been glaringly incomplete, indicating either a deplor-
able lack of scientific observation, or failure on the part of the writers
to appreciate the increasing necessity for careful and detailed reports
in such cases.  The grosser and more evident facts with reference to
diagnosis have already been well established, but the refinements in
diagnosis which are going to make it possible to detect the occurrence
of this complication at a much earlier stage and in a much larger pro-
portion of the cases are still lacking.  The question of general peri-
tonitis ought not to enter at all into the consideration of perforation.
Many of the pathognomonic signs, so-called, of perforation are now
known to be merely an indication of general peritonitis.  It is only by
keeping these two conditions distinctly separated in the general medi-
cal mind that the diagnosis of perforation is to be more frequently and
more accurately made, and it is only by strict and careful attention
from now on to the refinements of diagnosis that we shall be saved the
humiliation of operating for perforation and so frequently finding
extensive peritoneal infection.  Much improvement in operative tech-
nique at the present time cannot be expected, as this has already
reached as advanced a stage of perfection as our present surgical
knowledge will permit.  Improvement is to be looked for almost
entirely along the line of early and accurate diagnosis, which can only
be the result of careful clinical observation, and what is of equal or
even greater importance, of accurate pathological study.  The path-
ology of these cases, especially the information afforded by extended
post-mortem examinations in unsuccessful cases, has been even more
neglected than the clinical study, whereas the whole question of prog-
nosis and of the causes of death depend absolutely upon post-mortem
findings.  With but relatively few exceptions it has been assumed that
the mortality following operation has been due to general peritonitis.
It cannot be denied at the present time that this is not for the most
part a correct view, but the comparatively few post-mortem examinations
recorded certainly indicate that a good many of the unsuccessful cases
die from causes entirely independent of the operation, and which at the
present time are beyond means of control.  It is in the hope of stimu-
lating interest in the more uncertain points of diagnosis, and especially
in the pathological knowledge of these cases, as well as affording some

definite suggestions for accomplishing these objects, that the present article is presented. Many of the observations contained in this paper have been suggested by cases of typhoid perforation studied at the Lakeside Hospital in Cleveland during the last four years, several of which were reported by the writer from the surgical clinic of the hospital in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1902, vol. cxxiii. p. 38, " Laparotomy for Perforation in Typhoid Fever."

It may seem at first that it requires considerable temerity to speak of the diagnosis of typhoid perforation from a purely surgical standpoint. The view of the medical profession, however, has changed so radically with reference to the treatment of perforation, that it may almost be said to come under the head of a surgical rather than a medical complication, in the same manner in which appendicitis is now brought to the observation of the surgeon, not solely at a time when operation is immediately demanded, but for the sake of diagnosis in doubtful or somewhat obscure conditions. Surgical aid in the diagnosis of appendicitis has become of the utmost value, and we feel equally certain that much the same consideration will prevail with reference to typhoid perforation. It is largely on this account that the surgical interest in typhoid fever in general has recently become so manifest. The physical conditions of the abdomen are often so altered during the course of typhoid fever that the surgeon who is unfamiliar with the typhoidal abdomen is utterly incapable of giving a well-considered opinion in cases of suspected perforation. It was in view of this fact that Dr. Osler, a few years ago, so strongly urged the desirability of surgical observation of the typhoid cases at the Johns Hopkins Hospital, and it is largely on account of the lack of opportunity for such observation among surgeons in general that so little has been done on the subject outside of large hospitals. The desirability of surgical familiarity with the abdominal conditions in all stages of typhoid fever cannot be too strongly urged, and its importance cannot be over-estimated.

ETIOLOGICAL CONSIDERATIONS. In considering the subject of intestinal perforation in typhoid fever, there are a number of points in the etiology of the condition which have already been determined with all the accuracy that is desirable, and which can be dispensed with in a few words. The *time at which the perforation occurs*, so far as diagnosis is concerned, is of no consequence. It most frequently occurs during the third week, but in one of the Lakeside series there were very marked suggestions of perforation in one case on the fifth day of the disease, although no perforation was found, and in another case general peritonitis had followed a perforation occurring on the sixth day, as nearly as could be made out from the history. It may occur

late in a prolonged convalescence, or in a relapse, so that from a standpoint of diagnosis the stage at which the patient has arrived in the illness must be entirely overlooked. The time of perforation is of much consequence, however, with reference to the general condition of the patient and to the way in which operation is borne, as will be mentioned later. The *severity of the fever* can be overlooked entirely in diagnosis, except for the fact that diagnosis is more difficult in severely sick cases, where one scarcely ever finds the indications so marked. It is the opinion of Dr. Osler that it occurs more frequently in severe cases; but medical opinion in general is quite divided, and from the study of the reported cases one is certainly justified in a conservative opinion. It certainly appears to occur about as frequently in mild as in severe cases, and in any event it occurs so frequently in both classes that the mildness or severity of the disease can be entirely laid aside with reference to diagnosis. The matter of *constipation and diarrhœa* is of little consequence in diagnosis, the cases being so equally divided that these conditions can also be overlooked. The question of *age and sex* is of slightly more importance, but this also can be overlooked almost entirely. It occurs much more frequently in young adults, but three or four cases have been reported in children under fifteen years. It also occurs much more frequently in males than in females. Neither of these conditions can influence the diagnosis to any appreciable degree, however, except that one might be justified in delaying a little longer in cases of young children. It is of somewhat curious interest that only two instances of operation for perforation in a negro have been reported, and that in only one of these was perforation actually found. The question of *intestinal hemorrhage* is of somewhat more importance, but mainly from the fact that its occurrence at the time is very apt to mask or simulate perforation and render diagnosis much more difficult. As an etiological feature, however, antecedent to perforation, we believe it can be entirely overlooked. The occurrence of hemorrhage is purely fortuitous, and depends solely upon the chance of the ulcerating surface encroaching upon a vessel of considerable size. It cannot be assumed that the ulcer is approaching the peritoneal surface more rapidly on that account, or that the process will even eventuate in perforation merely because the hemorrhage has occurred. A comparatively small number of the reported cases of perforation have been preceded by hemorrhage, and it is only a small percentage of the cases of hemorrhage that have eventuated in perforation. In instances where the relation is suggested it is almost invariably a mere assumption that hemorrhage has come from the particular ulceration that has gone on to perforation. So that in considering the diagnosis of perforation we think one can entirely overlook as etiological factors the period of the disease in which the perforation

occurs, the severity of the disease, the occurrence of constipation or diarrhœa, the question of age, sex, and color, and the occurrence of hemorrhage from its purely etiological standpoint.

SYMPTOMS AND SIGNS OF PERFORATION.  In considering the *symptoms and signs* of perforation we believe it is of the utmost importance *to preserve a sharp distinction between the two*.  Some of the signs of perforation are doubtless always present, although possibly unobserved or misinterpreted.  The amount of dependence one can place on symptoms, however, depends entirely upon the mental condition of the patient and his appreciation of sensations.  The patient whose faculties are moderately alert can afford very material aid through his perception of pain and his own conception of being very much worse or very much better.  In proportion to the amount of apathy so often present to a greater or less degree, these sensations are much less acute, and the patient's ideas regarding himself are of much less consequence.  In deeply apathetic or delirious cases the question of symptoms must almost invariably be largely or entirely set aside.  Consequently in the latter class of cases, which are almost always the severely sick cases, one must rely almost entirely upon physical signs and phenomena.  As in so many other conditions, in the cases in which one is most desirous of making an early and careful diagnosis, the means at hand for making this diagnosis are much more strictly limited than in less severe cases where one can risk a little larger margin of error. It is thus evident that in most severe cases one is forced to be more radical in his diagnosis and establish the presumption of perforation on somewhat less sufficient grounds.  These two distinctions, then, between signs and symptoms on the one hand, and the clear-minded as against the apathetic and delirious patients on the other, at once assume proportions of the very highest importance, and it does not seem to the writer that these considerations can be too strongly urged.  These are distinctions to which we feel justified in making frequent reference.

*Symptoms*.  In considering first the symptoms of perforation one finds for consideration pain, sensitiveness, the sensations associated with systemic shock, and the sensations of altered respiration.  These have been named in the order of their relative importance in the vast majority of cases in which the sensibility of the patient is sufficiently acute to make them of any use whatsoever.

*Abdominal pain* is by far the most important symptom, and if present demands the utmost consideration in forming a diagnosis.  This is especially true where the patient has been comparatively free from previous abdominal complications and the symptom appears as a sudden, sharp, often agonizing sensation, quite circumscribed, located in the lower part of the abdomen near the median line or toward the right side; and especially if the pain remains severe and circumscribed for

an hour or more. Such a picture one can scarcely mistake, and with
a very slight suggestion along the line of physical signs one must feel
justified in making the diagnosis. The pain, however, may come on
gradually, commencing almost anywhere in the abdomen, but more
frequently starting near the median line, near or below the umbilicus.
If the pain is general at the start it usually becomes more closely con-
fined to the lower half of the abdomen within a short time. When
pain becomes more general after having been moderately well localized
at the start, it suggests rather strongly that peritoneal infection is pro-
gressing from a point of perforation. The pain, whether sudden or
general in its first manifestations, localized or diffuse, may at the
same time be either moderate or severe; in general it can be said that
the better localized the pain the more keenly it is appreciated, but the
distinction is of vastly less consequence than the fact itself that pain is
present. So that the occurrence of pain is a feature of the utmost
importance when present. The location of the pain, its limits, its
severity, the manner of appearance, and persistence are matters of
secondary importance, except possibly the last-mentioned feature. In
proportion to the degree to which these various features of the pain
are accentuated these secondary considerations of pain may be said to
be of importance, but the absence of such accentuation must be almost
entirely overlooked in arriving at a diagnosis.

*Sensitiveness* is, of course, very closely allied to pain, and may almost
be considered as a less strongly marked manifestation of the same sen-
sation, so that many of the things mentioned with reference to pain
are true to a less degree with reference to sensitiveness. All patients
with abdominal pain are sensitive, but one is often obliged to rely con-
siderably upon sensitiveness as a symptom in the absence of pain. The
limits of sensitiveness are usually more narrow than those of pain, and
on this account it is sometimes of aid in assisting the patient to more
definitely locate his pain. Localized pain is accompanied by localized
sensitiveness, but diffuse pain is not infrequently associated with cir-
cumscribed sensitiveness, and this fact is often an aid of considerable
importance. Spreading sensitiveness is open to the same interpretation
as spreading pain, and is if anything a little more to be relied upon.
The occurrence of sensitiveness is more common to the lower half of
the abdomen or to the entire right half. Its frequent occurrence in
the right lower quadrant, to which attention has been strongly called
by several writers, does not appear to exist in many cases. The truth
of this statement has been strongly suggested by the Lakeside series
and seems to be justified by the large proportion of reported cases.
The degree of accentuation increases the usefulness of sensitiveness,
also, as a symptom, possibly a trifle more so than in cases of pain; but
here again the characterizing features of sensitiveness are of only

secondary importance as compared with the presence of sensitiveness itself.

The *sensations associated with systemic shock* vary so greatly in different patients, and are so closely allied to certain signs to be mentioned later, that one is obliged to speak of them in a very general way. These sensations, general and varying as they are, however, in a responsive and clear-minded patient are worthy of careful consideration when present. Perhaps their meaning is best described by the expression so often used by the patient himself, literally or implied, of an " all-gone feeling," as if the " bottom had dropped out of him ; " a feeling vaguely described but strikingly realistic, that some serious catastrophe has occurred. It is doubtless this that sometimes causes in these patients the intensely anxious and apprehensive countenance not infrequently seen, the exact meaning of which they are unable to put into words. It is scarcely possible to speak of these sensations in more detail. Their presence is unmistakable and of considerable importance ; their absence, again, may be entirely disregarded in making a diagnosis.

The *sensations of altered respiration* are of little consequence compared with the other symptoms mentioned, or compared with respiration as a sign. The patient is apt to feel short of breath, and finds that his respirations for some reason or other must be largely costal. As a sensation it is present in almost direct proportion to the intensified characteristics of pain already mentioned, and in the absence of pain, at least in the absence of pain and sensitiveness, it does not exist. The symptoms of altered respiration are of so little consequence that they may be entirely disregarded.

*Signs.* But it is upon the signs suggesting perforation that one is forced to rely largely, and in apathetic and delirious cases one must rest his diagnosis upon these signs almost absolutely. Here, however, it is necessary to draw the distinction even closer between perforation and general peritonitis, and keep in mind that the diagnosis of general peritonitis is not the diagnosis of perforation. And against maintaining this distinction one cannot with propriety set the fact that both these conditions at times are very bizarre and misleading in their manifestations, and that occasionally the postmortem examination reveals a condition of which the manifestations before death gave absolutely no recognizable indication. These signs suggesting perforation include, first, indications gathered from the abdominal examination alone, such as muscular resistance, the presence of gas within or outside of the intestine ; and, second, certain general systemic indications, such as vomiting, altered respiration, temperature, pulse, altered blood conditions, and general systemic shock.

*Muscular resistance* is, we believe, the most important of all these signs. It is a sign of the utmost importance in almost any acute intra-

abdominal condition, and its reliability can rarely be questioned with impunity. It indicates very clearly that the abdomen is trying to protect itself against injury from the outside, and is a condition largely independent of the volition of the patient. The presence of pain and sensitiveness is, to be sure, usually associated with muscular resistance to a greater or less degree, but the same patient, if he is deeply apathetic or delirious, and abdominal protection is still needed, would show muscular resistance. This muscular resistance is not infrequently general, but in cases of perforation in typhoid fever, since the lesion is almost invariably located in the lower half of the abdomen or on the right side, the resistance is accentuated in these localities. Its usefulness is impaired to an inexperienced observer, however, in that many cases of uncomplicated typhoid show a varying amount of muscular resistance which must not be mistaken by one seeing the case for the first time. Here, again, is a very striking example of the necessity for surgical familiarity with the abdominal conditions in uncomplicated typhoid, and also of the great desirability of having typhoid cases under frequent surgical observation. Muscular resistance is probably never absent in perforation. If resistance was present before perforation it is probably always increased, and in such cases an accurate estimation of the degree of increased resistance is of great value.[1]

*Distention and tympany* from gas within the intestines are signs of no consequence with reference to perforation *per se*. Their absence is of equal inconsequence. As signs of spreading peritoneal infection, however, they are both of well-known and merited consequence and need not be discussed here. They are confirmatory evidences only in so far as one has been willing to run the risk of spreading infection secondary to the perforation. If there was gas in the intestines previous to perforation, as is frequently the case, it would not be increased by the accident; if the abdomen was soft and there was no distention one would not find a sudden accumulation of gas when perforation occurred. So that aside from the fact that distention and tympany may tend to obscure the diagnosis and render it more difficult they can both be set aside entirely with reference to the diagnosis of perforation itself, and are confirmatory only in proportion to the degree of spreading infection.

The presence of *abdominal gas outside the intestine*, however, if its presence can be demonstrated with certainty, is practically a proof of

[1] The presence and significance of muscular spasm have been receiving considerable attention of late. Muscular spasm is mentioned in comparatively few reports, and has doubtless been overlooked in many instances. The data is insufficient to judge with any degree of accuracy as to the frequency of its occurrence, but it is probably very often absent. We feel it to be a sign not infrequently confused with voluntary muscular contraction, and believe with Munro ("The Clinical Diagnosis of Typhoid Perforation," Boston Medical and Surgical Journal, February 5, 1903, vol. cxlviii., No. 6) that at the present time it is often difficult to properly estimate its significance.

perforation. Such evidence is usually sought through obliteration of the liver dulness. This manifestation, however, is a matter of such uncertainty that it renders the interpretation of the sign of practically no value. The obliteration of liver dulness has been demonstrated again and again to be due to a distended colon or small intestine as well as to free abdominal gas, and in several cases in which diagnosis was considered practicaly absolute on account of this sign, no perforation was found. The absence of altered liver dulness is, of course, a matter of absolutely no consequence in diagnosis, and in cases where the liver dulness is altered to an appreciable extent, it is quite impossible to say whether it has been effected by free abdominal gas or distended intestine. If the liver dulness is altered one may be justified in being suspicious of the circumstance, but we feel he is unjustified in any further assumption.

*Nausea and vomiting* occur so infrequently that they are of little aid in the diagnosis, and their absence may be entirely set aside. They are more frequently associated with cases in which there is severe pain, and in these cases are probably open to the same interpretation as nausea and vomiting under any condition of severe abdominal pain. They are also seen, however, as manifestations of severe systemic shock, but in such cases the presence of shock is so manifest that one need not look for the confirmatory evidence of vomiting. They occur in less than 25 per cent. of the cases. Their presence is of slightly confirmatory value only.

*Altered respiration* is a sign of consequence, and is probably to be interpreted as muscular resistance, namely, a means of protecting the abdomen. The prevailing type of respiration where perforation has occurred is almost invariably distinctly thoracic. This type of respiration is also seen in severe cases of typhoid with distention and rigidity, but the phenomenon is considerably accentuated when perforation occurs. It was a very striking sign in all the Lakeside cases.[1] It is rather more evident, to be sure, in clear-minded patients with considerable pain, assuming somewhat the quality of a symptom; but it is sufficiently recognizable as a sign alone where the mental condition of the patient is to be entirely disregarded. The rate of respiration, also, is nearly always more or less increased, but is of largely secondary consequence. If the patient is in pain, respiration may be unduly increased on this account alone; if he is insensible to pain, the restricted respira-

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[1] We were considerably surprised to see in a recent report of eight cases of perforation, by McCrea and Mitchell ("Surgical Features of Typhoid Fever," Johns Hopkins Hospital Reports, 1902, vol. x., Nos. 6, 7, 8, and 9), that the observation of altered respiration had been very inconstant, and was apparently of indifferent significance. Our observations have been so constant and well borne out, however, that we feel in no way inclined to belittle the frequency or significance of the sign.

tory excursion will necessitate somewhat more rapid breathing. Altered respiration, then, of the costal type warrants much the same assumption as muscular abdominal resistance, and we believe this alteration can be found in practically all cases if sufficiently well observed. As this alteration is largely relative it is probably less reliable than muscular resistance, and as it is open to the same interpretation its practical value, aside from being merely confirmatory, is not great. Its absence, however, as in the case of muscular resistance, must be considered of considerable importance.

*Alteration in temperature* may be of some positive value, but the absence of such alteration must be set aside entirely in making a diagnosis. An accompanying chill is of rather infrequent occurrence. Two of the Lakeside cases showed no alteration in temperature, and many other reported cases are equally negative in this respect. Many cases will show a rise or fall generally not exceeding 2° F., which, when considered with the usual irregularity of the typhoid chart, must be admitted to be of little value. A very decided drop in temperature, as is sometimes seen in hemorrhage, is rather less frequently met with in perforation, we believe, than has been generally supposed. As an indication of spreading infection the value of altered temperature has long since been well established, as was mentioned also with reference to distention and tympany; but as an indication of perforation itself the matter of altered temperature may be very largely overlooked.

The *pulse* is an indication of greatest importance. It is, of course, an evidence of systemic shock accompanying perforation, but is a matter of such consequence that it deserves special mention. One can almost invariably expect a rise in pulse that is quite marked, perhaps twenty beats or more, the alteration occurring rather suddenly. This rise in pulse is affected in a measure by the increased respiration, but is almost always too marked to be accounted for entirely on such grounds. The quality of the pulse also is markedly altered, the tension being reduced, and the pulse rendered readily compressible. These strikingly distinctive changes in the rate and quality of the pulse are, of course, less strongly marked in more severely ill cases, in which the pulse is already rapid and the quality poor, but even in such cases, to one familiar with the daily condition of the patient in question, the relative alteration is evident. It may also be of some aid in differentiating between shock and hemorrhage, as alteration in rate and quality is likely to be more gradual in hemorrhage; it is a distinction, however, that is by no means always recognizable, but may serve as a somewhat confirmatory observation. Sudden marked alteration in rate and quality, then, is an indication of great importance.

Definite knowledge regarding *altered blood conditions* occurring in typhoid fever is so meagre that we feel that little reliance can be

placed upon it in making a diagnosis of perforation. This may appear at first sight to be a rather striking and radical statement. In the large proportion of cases it is very doubtful if *the white blood count* is affected by the perforation itself. It is true that in many instances a leucocytosis is observed to follow perforation at an interval of anywhere from one to six hours; but, on the other hand, in a very considerable number of cases no such leucocytosis is observed. It has also been observed that moderately sudden and quite extreme leucocytosis occurs in patients in whom perforation was supposed to exist, when operation showed definitely that none had occurred. One of the Lakeside cases showed such a rise from approximately 8000 to 50,000. It has been assumed by some and considered demonstrated by others that following perforation there is a "wave of leucocytosis" extending over a period of a few hours, and that in cases where no leucocytosis is observed the observation has been made at the close of this wave. Some cases show this condition, others do not. Whatever one's belief regarding it may be, it is known to be a certainty that the leucocytic equilibrium in man is very easily disturbed to a greater or less extent. Some of the causes that at times effect this disturbance are known with a moderate degree of certainty, but the number of causes with which we are somewhat acquainted is probably very small as compared with the number of causes for which we are utterly unable to afford any adequate explanation at the present time. Slight temporary differences in the white blood count are usually beyond explanation, and while it may be assured that such temporary flights occur in perforation it is an assumption that must be based upon far wider and much more accurate observation than has been made thus far. These waves of leucocytosis have been demonstrated to exist in many conditions, and for that matter in supposedly normal individuals, which had they occurred in conjunction with symptoms suggesting perforation might be assumed to be due to that cause. One such set of observations has been made by Cabot, Blake, and Hubbard in an article on "A Study of the Blood and Its Relation to Surgical Diagnosis," *Annals of Surgery*, vol. xxxiv. p. 361. These views are based upon the observation of only ten cases, to be sure, four of which were typhoid fever, but they are as extended and certainly more accurate on the whole than any observations in favor of the leucocytic wave theory in perforation, and serve to put the subject where one is unable to attach to it much diagnostic importance at the present time. What may, however, prove to be of some consequence is a steadily increasing leucocytosis reaching a well-marked maximum, which is attained after a considerably longer period than the height of the so-called wave. The interpretation of this increase, however, is largely an assumption; it may be due to spreading infection which has not yet become sufficiently marked to cause the fall in the

number of leucocytes not infrequently seen in cases of extensive peritoneal infection. Be this as it may, it must be admitted to be of relatively small practical importance, for if these cases are to be saved one must not wait for a well-developed leucocytosis from any such cause. There is a great though apparently decreasing tendency to overestimate the value of leucocytosis in surgical abdominal conditions at the present time, and we feel that this is an example. The irregularity noted in the blood examinations in cases of demonstrated typhoid perforation is so great that the subject needs far wider and much more accurate study than has thus far been given. But while from the standpoint of diagnosis the question of leucocytosis must be largely set aside, from the standpoint of careful and complete observation of cases the importance of such examination cannot be overestimated. The subject may have possibilities; before leaving it the absence of such possibilities must be thoroughly demonstrated.

Alteration in the amount of *hæmoglobin* and the number of *red blood corpuscles* in these cases is a matter that has been almost entirely overlooked, but from a theoretical standpoint it would appear to be of somewhat more consequence than the white count. The most difficult cases for diagnosis are those in which the decision lies between hemorrhage and perforation. If the diagnosis of hemorrhage is incorrectly made, and instead of this perforation has occurred, the desirable opportunity for operation is lost while waiting for the demonstration of hemorrhage through the bowel discharges. It may be possible to make use of the red count and the estimation of hæmoglobin as affected by hemorrhage to aid in the differential diagnosis in these cases. The white count can be of little aid in this differentiation. It is felt that some careful observations along this line will prove valuable.

*Systemic shock* is probably always present, although not always recognized, and is an indication of the very greatest importance. The condition is usually so evident and its indications so readily recognizable that it is scarcely necessary to consider it in detail other than to insist on its importance. Altered respiration to a slight degree possibly, and especially alterations in pulse, temperature, and blood are indications of general systemic change. The pallid countenance, the drawn facial expression, slight cyanosis of lips and finger-nails, the sudden occurrence of perspiration, and the slight tremor that is sometimes present, together with the altered pulse and temperature, make a very striking picture when well marked. Here, again, however, in proportion as the organism is deeply affected by the disease itself, the margin of vitality susceptible to even the severest degree of shock is narrow, and the system may be so deeply affected that it fails entirely to respond in any appreciable degree to the shock received, and the catastrophy passes unrecognized. It must be kept in mind, however, that this is

said solely with reference to the severity of the infection, and is entirely independent of the mental condition of the patient. Shock is distinctly recognized by physical, not mental demonstrations, and if any reactionary power remains in the organism the condition can be recognized in spite of delirium or apathy. This condition of systemic shock was observed in all of the Lakeside cases. In one case with severe infection and moderately well-marked shock no perforation was found, and the cause of the suddenly altered condition was never demonstrated.

In summary, then, the signs and symptoms upon which one is forced at the present time to rely mainly in making a diagnosis of perforation are *pain, sensitiveness, muscular resistance, altered respiration, alteration in rate and quality of the pulse, and evidences of systemic shock.*

DIFFERENTIAL DIAGNOSIS. The question of differential diagnosis is a matter upon which there is little to be said with satisfaction, owing largely to our fragmentary and quite indefinite knowledge of the causes of pain during the course of typhoid fever. Pain must be considered a most important symptom, and at times the most important feature in making the diagnosis of perforation, but at the same time it is the indication which most often leads us astray. A most instructive and commendable paper by Dr. Thomas McCrae, " Abdominal Pain in Typhoid Fever," *New York Medical Journal,* May 4, 1901, vol. lxxiii. p. 749, is perhaps the most valuable article of its kind that has occurred in the more recent literature. His report is based upon the analysis of 500 cases at the Johns Hopkins Hospital, in which it was found that only two-fifths of the patients were free from pain or tenderness; one-fifth showed tenderness only, while two-fifths showed pain sometime during the attack. Of this number there were only 13 cases of perforation, while in 70 cases there was no discoverable cause. It must be admitted that in a large proportion of cases in which the existence of perforation has not been demonstrated at operation, the causes of the indications leading to the diagnosis have not been discovered, and in instances in which the causes have been assigned it was largely an assumption. Among these causes, known or supposed, are diaphragmatic pleurisy, pneumonia, iliac thrombosis, appendicitis, peritonitis from undiscoverable causes, intestinal obstruction, suppurating mesenteric or retroperitoneal glands, cholecystitis, and intestinal hemorrhage.

Regarding *pleurisy* and *pneumonia,* they have both been known to be associated with abdominal pain, the entire aspect of the case resembling very closely that of perforation. If the pneumonic process is not sufficiently near the surface to be recognizable, one can have little hope of avoiding the mistake. A careful pulmonary examination in all cases is the only possible precaution. Such cases are, however, fortunately, very rare. *Iliac thrombosis* is usually associated with sen-

sitiveness in the groin and for a varying distance along the course of
the femoral vein, and a careful examination may reveal this cause of
a misleading symptom and should always be carefully kept in mind.
*Appendicitis* occurring during the course of typhoid fever can very
rarely be differentiated from perforation occurring in or near the
cæcum, and there is fortunately no need for so doing, as the indications
for operative interference are so nearly identical.  *Peritonitis* without
discoverable cause has been mistaken for perforation, but can scarcely
give the early appearances of perforation; in either event, however,
immediate interference would be indicated.  *Intestinal obstruction* has
simulated perforation, but here, too, the instances in which it would
simulate the early symptoms of perforation must be extremely rare,
while the indications for exploration would be equally certain.  The
considerations of consequence in connection with appendicitis, periton-
itis, and obstruction with reference to perforation are not so much in
relation to the difference in diagnosis, but that the conditions must be
kept in mind as possible causes of the symptoms and signs in cases in
which no perforation has been found.  The same may be said of cases
of *suppurating mesenteric or retroperitoneal glands;* this condition can
scarcely be mistaken for perforation pure and simple, but has been
mistaken for resultant indications of perforation due to spreading
infection.  *Cholecystitis* has simulated perforation very closely, as in
the case reported by Dr. H. B. Allyn, "Typhoid Fever, with Perfora-
tion of the Colon and Gall-bladder; Operation; Death; Autopsy,"
*Philadelphia Medical Journal*, August 3, 1901, vol. viii. p. 193.  In
this case no perforation was found, the existence of cholecystitis was
not discovered at the operation, and the cause of the misleading indi-
cations was found only at autopsy.  In such cases, however, the pain
is usually high in the abdomen, and is very likely to be associated with
slight jaundice or a trace of bile in the urine.  Here, again, however,
the important consideration is not the diagnosis, but the possibility of
overlooking such a condition where no perforation is found.  From
*hemorrhage*, however, differential diagnosis is of the utmost importance.
Less than half of the cases of hemorrhage are associated with pain, and
it is probably the proportion is small in which perforation might
be reasonably suspected.  The diagnosis is of importance not so much
because hemorrhage sometimes suggests perforation, but because the
indications of perforation itself are sometimes attributed to hemorrhage,
which is a mistake of the utmost gravity.  Where the two conditions
do suggest each other it is a diagnosis of the greatest difficulty, and in
the present state of our knowledge there is relatively little to aid one.
The pain and sensitiveness may be the same, the signs themselves may
be almost identical.  Alteration in the rate and quality of the pulse,
however, may be more gradual in hemorrhage, but the difference is

purely relative and not always of assistance. The evidences of systemic shock are usually more severe in perforation, but this is also a relative difference and merely a suggestion. As the case progresses the diagnosis of hemorrhage is usually rendered clear by the subsequent appearance of blood in the stools, but if perforation is strongly suspected one cannot be justified in delaying for this confirmation of the diagnosis of hemorrhage. The reduction of hæmoglobin and the number of red corpuscles, it is strongly believed, may be of material aid in differentiating these two conditions, as has been suggested by McCrae, and was of demonstrated value in one case at the Johns Hopkins Hospital. We feel that this is a most important subject, and would urge that it be widely investigated and reported for the sake of accumulated statistics. But when all is said it must be admitted that differential diagnosis between perforation and hemorrhage is sometimes extremely difficult and misleading, and in such instances one must feel justified in diagnosing perforation rather than hemorrhage, since the gravity of delay in perforation far exceeds that of exploration.

It may be well to mention here several things not already noted which may obscure or aid in the diagnosis. To one who is familiar with the not infrequent effects of tub baths, especially in severely ill cases, it would be suggested at once that the abdominal pain, muscular rigidity, and varying degrees of systemic shock sustained might lead one astray in a case where perforation was suspected or even where no such thought had been entertained previously, if the effects of tubbing were unusually marked. It is, therefore, a wise precaution in suspected cases to substitute sponge baths, in order that the diagnosis may not be obscured by ever so slight an alteration in the patient's condition from other than the suspected cause. In one of the Lakeside cases the sudden change in the patient's condition was thought to be due to the effects of the tubbing, and caused a disastrous eight-hour delay before operation. Again, in administering morphine in cases of hemorrhage one is courting danger on one hand while attempting to forestall it on the other. It is at once evident that in cases suggesting both perforation and hemorrhage the diagnosis should be clearly defined if possible before administering morphine. There are occasionally cases, however, in which one feels obliged to give morphine regardless of the consequences. One other suggestion which we have not seen mentioned elsewhere seemed at the time to be of material aid in the diagnosis in two of the Lakeside cases, in one of which perforation had actually occurred, while in the other operation was delayed and the case recovered. In both of these instances the question was raised whether the rather moderate abdominal pain might not be due to flatus. A small glycerin enema administered in each instance was expelled by both patients with the evacuation of considerable gas. In the case of actual

perforation no relief from the pain was experienced, while in the case recovering without operation the pain was considerably though ·not entirely relieved.    It is a procedure that is scarcely applicable in cases of suspected hemorrhage, but may occasionally afford information of ·.. more or less value where perforation is suspected independently of hemorrhage.

It may be permissible to consider in this connection the so-called '' pre-perforative stage,'' upon the existence of which as an absolutely recognizable condition Dr. Cushing, of Baltimore, has been so, persistently insistent.    In the *Johns Hopkins Hospital Bulletin*, November, 1898, No. 92, p. 267, he defines his position as follows:    '' Under the ' pre-perforative ' stage let it be understood that the whole period is included between the first involvement of the serosa with the customary formation of adhesions at this point, until these adhesions, which may for the time constitute the floor of the ulcer after the serosa has given way, have themselves become broken down and general extravasation has taken place.''    What he refers to is a pre-extravasation and not a pre-perforative stage, and this distinction the writer himself mentions in a subsequent paper.    That adhesions form in all cases of perforation is probable in spite of the fact that they cannot always be demonstrated at operation.    That every case of perforation has what may be called a pre-perforative or pre-extravasation stage is too evident to need mention, just as anything that occurs has a pre-existent condition ; but when the same writer mentions it as a '' definite recognizable condition '' he is insisting on a refinement of abdominal diagnosis that is quite beyond the possibility of recognition with any degree of certainty.    The impossibility at the present time of recognizing a distinction depending upon the thickness of the peritoneum is self-evident. An early diagnosis is the *ne plus ultra* in perforation, and doubtless in some of these cases one may feel satisfied he has found the condition mentioned by Dr. Cushing, but it is seldom to be hoped that one will strike the exact time of perforation with such accuracy.    It is firmly believed that the best that can possibly be hoped for is the possibility of operating upon these cases within a considerably wider limit than Dr. Cushing urges, a little before or a little after the catastrophe has actually occurred, and the cases in which one is able to place his operation between the involvement of the peritoneum and actual extravasation are, we believe, purely fortuitous and not a matter of judgment.

OPERATIVE TREATMENT.    It is hardly necessary any longer to urge that the treatment of typhoid perforation is solely operative.    It may not be always possible to operate, but when the diagnosis of perforation is once made one can no longer consider the patient as being under treatment if operation is not employed.    So far as the patient is con-

cerned, however, it can be safely said that operation should be resorted
to in all instances.   This is the only reasonable ground in even the
most desperate cases.   The list of recoveries contains a number of the
most hopeless instances of surgery as a last resort, notably the remark-
able case of Dr. Abbe, *New York Medical Record*, January 5, 1895, in
which operation was performed sixty hours after perforation, and in
which two pints of extravasated fecal matter were removed from the
abdominal cavity; also the case of Dr. Champlin, No. 155 of Dr.
Tinker's series, published by Dr. Keen in his article already mentioned,
in which the interval between perforation and operation was estimated
at three days; and the case of Dr. Pearson, *British Medical Journal*,
1899, vol. i. p. 1097, in which recovery followed operation nine days
after perforation was thought to have occurred, although in this instance
there was a localized abscess about the cæcum, the case resembling
more a slowly progressing appendicitis.

The *time when the operation should be performed*, that is, the number
of hours after perforation, is a matter upon which statistics seem
strangely at variance with common sense and experience.   Cases of
perforation are always associated with a greater or less degree of shock.
To operate during the severity of this condition can scarcely be con-
sidered wise unless the period of shock is unduly prolonged.   The
diagnosis having been made, however, the matter of an hour or two of
heat and stimulation in the severest cases will serve to get the patient
in as good condition for operation as one can hope.   If the systemic
shock is quite inconsiderable we need not delay even this length of
time.   If the period of shock is prolonged in spite of treatment, we
believe that the danger of spreading infection will far exceed any
possible benefit derived from delaying in the hope that the patient's
condition will improve.   It is owing to the deplorable lack of post-
mortem examinations that we are obliged to assume this position
instead of accepting it from demonstrated facts.   The cause of death
in the vast majority of reported cases has not been accurately ascer-
tained, and where stated has been merely a clinical assumption.   The
number of autopsies obtainable from the reports is far too small to
justify any conclusions.   It is probably true, however, that general
peritonitis is the cause of death in the majority of fatal cases operated
upon at an early date, and in a very large proportion of cases in which
operation has been delayed.   It must certainly be admitted that a case
dying of general peritonitis following early operation could not possibly
have been saved from this catastrophe by delaying a number of hours.
The statistics of Dr. Westcott and Dr. Tinker, published by Dr. Keen,
show that the largest percentage of recoveries follows operations per-
formed during the second twelve hours after perforation.   We cannot
but feel, however, that these statistics, convincing as they first ap-

pear, are quite misleading. They are largely made up of the older cases, in most of which operation was long delayed and among which the recoveries were largely instances of fortuitous and unlooked-for good fortune. The fact, also, already mentioned, that the cause of death in all but a few of these cases was never definitely known affords a possibility of error that renders the statistics practically useless. In the more recent cases recovery has been much more frequent among those in which operation was early performed. But even here, again, unless sufficient interest is exercised to demonstrate positively the cause of death in unsuccessful cases, the decision of this question must be largely a matter of general experience and not scientific demonstration.

The nature of the *anæsthetic* will often prove to be a matter of consequence, especially whether one will employ local or general anæsthesia. There are frequently serious objections to both, but we cannot at all subscribe to the feeling of certain writers who claim that local anæsthesia should be employed in all cases, and that the use of general anæsthesia is a deplorable mistake. By the employment of local anæsthesia it has been thought to obviate entirely the additional shock of the administration of a general anæsthetic. In some instances this is so, in others it is purely an assumption. It is too often the case that what may be spoken of as purely operative shock is largely attributed to the use of a general anæsthetic, and no one will maintain that laparotomy under cocaine, in which the abdominal contents are disturbed, is entirely relieved of shock by the omission of a general anæsthetic. The mental anxiety, worry, and dread incident to a laparotomy under local anæsthesia in a hardy, strong individual, or even in a patient whose sensibilities are dulled to no inconsiderable degree by the severity of the illness, is a consideration never to be overlooked and will not infrequently render the decision against local anæsthesia. What is to be accomplished is the greatest possible reduction of systemic shock to the patient incident to the operation, and in some instances this is best accomplished by local anæsthesia, in others by general anæsthesia. Stolid and more or less apathetic patients are more favorable for local anæsthesia. The amount of self-control an individual is able to maintain is a very uncertain indication, as the greatest self-control may sometimes be associated with extreme and very depressing mental strain. Even in those cases in which a local anæsthetic has been properly and successfully employed, it is doubtful if the extensive and careful abdominal irrigation usually required, can be as well accomplished in most instances without resorting to a general anæsthetic at this stage of the operation. As so much depends on the care and thoroughness of this part of the procedure, it does not seem always wise to complete it under local anæsthesia unless the indications are very direct.

One of the main objections to general anæsthesia is the fact that so much time is usually lost in getting the patient sufficiently under. This may be obviated by using chloroform after the administration of about one-quarter grain of morphine hypodermically; but what we feel will eventually prove a still more rapid and considerably safer method is the employment of nitrous oxide and oxygen followed by ether. By using the gas and ether alternately in getting the patient under, complete anæsthesia can be produced readily in one to two minutes, and the method is devoid of the unforeseen but ever-present dangers incident to chloroform. The prolonged use of nitrous oxide and oxygen alone may eventually displace the use of chloroform and ether altogether in these cases, but at the present time its usefulness and safety for prolonged anæsthesia has not been sufficiently demonstrated. When general anæsthesia is employed it is unnecessary to add that it should be given into the hands of one of very considerable experience, and the administration should be as light and as short as possible. One advantage of the general anæsthetic thus administered over local anæsthesia, which we feel is not always kept in mind, is the greater rapidity with which the operation can be done under general anæsthesia, and the considerable reduction of the exposure and handling of the patient, to say nothing of the added thoroughness with which the operation may be performed. The use of local anæsthesia in these cases is an extremely simple matter to one who has even a limited abdominal experience, but its usefulness and employment is something which should be carefully considered and not entirely assumed.

The requirements of operation are so direct and clear that the *technique* is simple, and the steps of the operation well defined and logical. As an operative procedure it has been so well developed that we can look for comparatively little improvement in this direction, and there is consequently much less of interest in this portion of the discussion. The *incision* in the right lower quadrant of the abdomen is the only logical opening in these cases, and the linea semilunaris opposite or a little above the anterior superior spine we believe to be preferable. The lower part of the ileum, the cæcum, and the appendix include the vast majority of perforations, and are, on the whole, most readily accessible through the incision mentioned. An additional advantage of this incision is the well-recognized fact that the search for perforation is best begun from the cæcum. The incision should be sufficiently generous, perhaps 8 to 10 cm. long, to allow a careful and somewhat visual exploration. It occasionally happens that the perforation is completely protected by well-formed adhesions and fecal extravasations prevented, as was the case in an operation performed by Dr. J. C. Warren, reported by Dr. R. B. Greenough, *Boston Medical and Surgical Journal*, May 8, 1902, vol. cxlvi. p. 491. If these adhesions

are blindly broken up through a small incision unnecessary fecal extravasation may occur, the danger of which, owing to the certainty of the infection, cannot be estimated.

After entering the abdomen the first *search for the perforation* should be made in the ileum immediately above the cæcum, as the vast majority of perforations occur in this portion of the gut. By far the best way of accomplishing this is by starting at the cæcum, a fixed point very quickly found. We feel that this is a very wise routine procedure to employ, since one knows accurately the exact location of the small intestine he is handling and avoids the discouraging loss of time almost invariably incident to a haphazard and undiscriminating inspection of coils of small intestine appearing in the wound. Starting with the cæcum, one should inspect the ileum for a distance of about one metre. There is no object in going above this unless one intends to search the entire intestinal tract. This search for the perforation can be hurriedly but carefully conducted if the incision is sufficiently large to afford even a limited view of the general field. It is usually considered wise to replace the coils of intestine within the abdomen as the search is made, although some feel, and not without reason, that keeping the explored portion of the intestine well covered with hot towels and finally replacing all the coils at once can be accomplished with less handling of the intestines and less incident shock to the patient. We feel it is wise to make this first hurried search of the ileum for the perforation only, which is immediately recognized if present, a more careful examination of the gut for very thin ulcers being made after the really serious features are corrected, providing the condition of the patient will permit. It also affords a comprehensive conception of the portion of the bowel almost invariably affected, and prevents the possibility of spending valuable time over relatively unimportant conditions. It is, therefore, well to make this entire rapid inspection of the bowel even before closing any perforation that may be found. It is a very simple matter for an assistant to retain the location of these perforations outside the abdomen with sponges. The *method of closure of the perforation* is relatively unimportant, but should always be done with silk; catgut alone has been demonstrated on several occasions to be insufficient. A short double row of continuous Lembert sutures is all that is required, and can be very rapidly placed without elaboration. Excising the ulcer before suturing is an utterly useless and time-consuming procedure. It is a rare exception to find an ulcer of such size that the suture encroaches to an important degree upon the lumen of the gut; in such instances the suture must be placed with greater care. If there are several neighboring or confluent perforations, or the integrity of a considerable portion of the gut is severely impaired by deep ulcerations not yet perforated, it is

wise to secure this portion of the intestine to the edge of the wound rather than consume time by resection or an elaborate method of suture, and to close the fistula subsequently.[1]    Having secured the perforation, if the condition of the patient permits, it is always wise to make a retrograde search of this last metre of the ileum for *deep ulcerations threatening perforation*.    These can be recognized with considerable accuracy by the trained touch.    Running the finger down over the bowel the dangerous areas are indicated by small, soft, circular places in the centre of a moderately large, thickened area.    The sensation is readily acquired by post-mortem examination of an ulcerated ileum, in which the observation can be verified by subsequently opening the bowel.    These areas when found should be reinforced by a running silk Lembert suture.    The cæcum and appendix being immediately at hand, it is well to give them a passing inspection.    One is scarcely justified, however, in removing the appendix unless it is seriously affected, and not in instances where it is "at all abnormal," as was recommended by Dr. Finney, in his article in the *Johns Hopkins Hospital Reports*.    If no perforation has been found in the search so far instituted, it is inadvisable to make further examination of the intestinal tract, excepting, possibly, the sigmoid flexure, which is occasionally, though quite rarely, affected.    Typhoid perforations in other locations are so extremely rare that one would lose many more patients in a prolonged intestinal search than in running the slight risk of having overlooked such a condition.

*Irrigation of the abdominal cavity* we feel should be somewhat prolonged and very thorough, even if there are no visible evidences of peritonitis or extravasation.    The stimulating usefulness of hot irrigation has been even urged in explorations where no perforation has been found, but at the present time one hardly feels inclined to irrigate in such cases.    In many instances this abdominal irrigation should be deferred until the inspection of the gut has been made, unless the inspection is seriously hindered by the amount or nature of the fluid present, in which case a rapid preliminary irrigation may be useful, the main irrigation, however, to be reserved until after the

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[1] Since the writing of this paper we have had occasion to feel that certain cases of rather widely distributed severe lesions may be suitable for resection. A recent case of the Lakeside series, not yet published, presented at operation two perforations and nine deep ulcers distributed over 40 cm. of the ileum. Two perforations and three ulcers threatening perforation were sutured, and a chance taken on the remainder, although the gravity of so doing was recognized. The patient died five days later, primarily from pneumonia. No further perforations were found, but two of the unsutured ulcers were saved from actual extravasation only by light adhesions. The presence of a slight beginning peritonitis not over a few hours old was apparently due to infection through the thin adhesions covering these two ulcers, and doubtless contributed to and would certainly later have caused the death of the patient. We feel that the patient would have stood resection of the affected area and anastomosis with a Murphy button, and on reviewing the case it is a source of deep regret that the procedure was not employed. We know, however, of no attempt at resection up to the present time.

treatment of the bowel. Salt solution is possibly preferable to sterile water, but either one will do. It should be about 115° F., copious in amount. This, we feel, is best and most wisely accomplished through one or several irrigating tubes without removal of the intestines, and should be especially thorough in the region of the pelvis and lumbar fossæ. It is often well to irrigate the pelvis first, introducing a large rubber tube which will take up a large part of the return flow; in this way one will not infrequently avoid general dissemination of a large proportion of the abdominal fluid and fecal extravasation which very frequently settles to the pelvis. If extensive peritonitis is already present, one must treat this complicating incident as such, and that will vary greatly according to individual belief. We feel, however, that the extensive intestinal manipulation sometimes advised in such cases is of doubtful wisdom unless the condition of the patient is unusually favorable. We would feel inclined to rely on thorough and prolonged irrigation of the abdomen without removal of the intestines, as this is about all such patients can endure. In many instances, to properly accomplish this irrigation to the best advantage, we feel that a general anæsthetic is advisable, although it is occasionally satisfactorily accomplished under local anæsthesia.

It may seem occasionally wise to close these cases without *drainage*, but such has certainly been felt to be the rare exception. It is possible that having the temerity to close these cases after thorough irrigation may add considerably to the recovery rate; such cases, however, should certainly be restricted to those in which examination of the abdominal fluid during the operation shows the absence of organisms, or, possibly, those in which only bacilli are found to be present; but the advisability of drainage is scarcely questioned at the present time. The way in which one drains will vary according to the operator's personal belief. Whatever the method, however, it seems advisable to drain the pelvis. In the Lakeside cases what proved to be a very satisfactory method was by means of glass drainage tubes leading to the pelvis, and along the side of the tubes in some instances gauze drainage was also placed. It seems wise, also, to leave the seat of perforation or doubtful portions of the bowel near the incision, introducing gauze drainage to this portion of the bowel in order, if possible, to forestall the disastrous consequences of insecure suture or subsequent perforation. Around the drainage the wound should be closed as completely as possible, as the granulating capacity of such patients is sometimes considerably reduced, although the healing of wounds by first intention seems to be rapid and secure.

While it is needless to say that the operation should be done as rapidly as possible, it must still be remembered that *these patients bear operation* much better than one would ordinarily be led to suppose who

had not had the opportunity for personal observation. The incision, the search for perforation, the repair of the bowel, can all be very rapidly and at the same time thoroughly performed, so that this portion of the operation may well be considered the minor part. The careful and thorough irrigation, however, is a matter that cannot be unduly hurried, although here the time can be somewhat diminished by having several irrigating tubes in use at the same time. This portion of the operation, while possibly consuming the most time, is the least depressing to the patient, as it is associated with a considerable degree of stimulation. We fear not a few cases are sacrificed through lack of proper irrigation, owing to the overwhelming desire of operators to complete the operation in as short a time as possible. We would urge the desirability of the utmost speed during the really operative part of the procedure, which is easily possible for any operator of moderate dexterity and good judgment, but would deprecate hurried and inadequate cleansing of the abdominal cavity. The superior ease and rapidity with which one can accomplish the operation under a general anæsthetic is often in marked contrast to the slow, painstaking procedure not infrequently required under local anæsthesia where the sensibilities of the patient are so keenly alive to what is going on, and this consideration, as previously mentioned, will not infrequently incline the operator to the use of general anæsthesia as of marked advantage.

The *subsequent treatment* of these cases presents nothing distinctive or striking, it only being necessary to keep in mind the requirements of the patient from the standpoint of a laparotomy on the one hand and that of typhoid infection on the other. While we do not mean to suggest that the treatment of such cases does not require the greatest care and judgment, it presents no distinctive feature which need be dwelt upon. One thing, however, is extremely desirable, namely, to keep constantly in mind the possibility of a subsequent perforation, and avoid as far as one is able the possibility of obscuring the manifestations of this occurrence in any way by the line of treatment.

The question of *exploratory incision* in rather doubtful cases of suspected perforation we feel is a matter of great importance and increasing interest. This has been most advantageously urged and considered by Dr. H. W. Cushing, and is, we feel, his most useful contribution to the surgery of these cases. It has been exceptionally well expressed in his article, " Sur la Laparotomie Exploratrice Précoce dans la Perforation Intestinale au cours de la Fièvre Typhoide," *Archives Générales de Médecine*, January, 1901. In instances where perforation is suspected, but the diagnosis cannot be considered as definitely made, exploration affords the only hope of avoiding the catastrophe of allowing a perforation to go unrecognized until more or less general infection

has occurred. Even at the present time it has been proven beyond a reasonable question that these operations when properly performed are practically devoid of danger and affect the condition and course of the patient to a scarcely appreciable degree, whether performed under local or light and rapid general anæsthesia. If no perforation is found the abdomen can be immediately closed, a collodion dressing applied and the baths resumed within a few hours, so that treatment of the patient need scarcely be interrupted. Such was the case in No. 4 of the Lakeside series. The impervious dressing necessary for continued tubbing is conveniently applied by using six or eight alternate layers of collodion and sheet wadding, each layer being a little larger than the one previously applied. It is well to use only half of the thickness of the ordinary sheet wadding.

Exploration was first suggested by Dr. Finney, who advised making a very minute incision for the purpose of taking cultures from the abdominal cavity. This method was employed in the Lakeside case mentioned, but the restricted nature of this exploration was considered a mistake, and can certainly be no longer recommended. One must now be able to detect more than the presence of free abdominal fluid or organisms within the abdominal cavity. The perforation may be protected by adhesions or the ulceration may be scarcely through the peritoneum, either of which conditions may occur without being discovered by such restricted exploration. If one is to look at all he should examine the ileum and cæcum with care; it will take scarcely more time and will afford information of consequence. It must be readily admitted that the very slight danger incident to a rapid, skilful exploration is not to be compared with the serious consequences of an unrecognized perforation. Considering this as an aid to diagnosis, it is largely along this line that we are to look for a considerably larger percentage of recoveries from perforation. It will necessarily result occasionally in a premature operation, but will add very materially to the number of lives saved.

In instances where no perforation is found, either with or without evidences of peritoneal infection, at once arises the question of how far one may feel justified in exploring the abdomen for such *other intra-abdominal conditions* as have been known to suggest perforation. This is a matter which will be decided entirely by the individual judgment of the operator, and must be affected to a greater or less degree by the condition of the patient. Where, however, one finds an abnormal intra-abdominal condition, as peritonitis, for instance, it seems hardly justifiable to limit the search for the seat of the trouble to a rapid glance at the ileum and cæcum. The appendix is so close at hand that its inspection should never be omitted. The detection of suppurating mesenteric glands is important for the sake of adequate disposition

of drainage. Exploration of the region of the gall-bladder may be accomplished without serious objection. The presence of intestinal obstruction may possibly be detected by a hurried examination of the intestine from several parts of the abdomen. Unless the indications are pretty direct, however, one would scarcely feel inclined to risk much time on this very remote possibility. The extent to which these explorations are to be pushed is a matter for much thoughtful consideration.

The advisability of *secondary operation* for subsequent perforation or other operative indications is no longer a matter of general question, but of individual judgment in each case. The remarkable vitality displayed in a number of reported cases in which two or more subsequent operations were performed, has established this point beyond reasonable question. Operative indications are to be followed, and can no longer be set aside, for the simple reason that the patient has already undergone one operation.

PROGNOSIS. At the present time it is extremely difficult to form even a reasonable idea of the prognosis in these cases. We know that it is affected by a number of conditions. In general, the recovery rate is higher among young people. The time during the disease at which perforation occurs has an influence, since the recuperative powers of the individual are altered at different times. Recovery is less frequently to be expected when perforation occurs during the height and severity of the disease, whether of a primary attack or in the midst of a severe recurrence. When perforation occurs early in the disease, before the vitality of the patient has been drawn upon to any considerable degree, the prognosis in general is better, and also during convalescence after the recuperative powers of the individual have begun to assert an advantage. The prognosis is always severely affected, of course, by the length of time the case has been allowed to go after perforation, the extent to which a spreading abdominal infection has occurred, and the bacterial nature of this infection. It is also largely affected by the judgment, skill, and dexterity of the operator. But when it comes to an estimation of the percentage of recoveries the figures obtainable from the present statistics are, we believe, absolutely unreliable. In Dr. Westcott's table, comprising the first 83 cases reported, the recovery rate was 19.3 per cent., while in Dr. Tinker's table, comprising, presumably, the next 75 cases reported, the recovery rate was 28 per cent., making an average recovery rate for the entire 158 cases of 23.41 per cent. This recovery rate is far below that obtainable under the present conditions of diagnosis and operative technique; but the prognostic suggestions afforded by even the most recent cases which the writer has carefully collected are, we feel, too inaccurate and undiscriminating to deserve mention. This analysis

affords a certain percentage of deaths associated with operation, to be sure, but many of the cases dying after operation bear no relation whatsoever to the true mortality in direct connection with either the perforation itself or the operation. This last statement has been most satisfactorily demonstrated by several post-mortem examinations in the Lakeside series. With but rare exceptions it has been impossible to draw this distinction in our study of recent cases owing to the incompleteness of the reports, but we are sure such a discrimination would alter materially our statistical mortality. Dr. Osler has divided these cases into three classes: those which recover from operation, those which die from causes immediately related to perforation and operation, and those which die from causes entirely unrelated to either. It is of the utmost importance that this distinction be kept closely in mind in forming an estimate of the mortality in these operations, but it is a distinction which, curiously enough, seems to have almost entirely escaped the thought of those attempting to form a statistical opinion of recovery and mortality. It is absolutely impossible to acquire the knowledge necessary to form this more accurate opinion without wide and accurate pathological observation and careful post-mortem examinations. An attempt was made by the writer to form such an estimate from the number of autopsies reported, but the number at present is so small and the reports are so fragmentary and inaccurate that the analysis has proved utterly worthless. Unless the operators under whose observation these cases are occurring can contribute generously to our pathological knowledge, any further reports are practically useless and might much better be omitted, since superficial reports only burden the literature without contributing to our present knowledge. Dr. Keen estimates that we can look forward to 30 per cent. of recoveries. The recovery rate at the Johns Hopkins Hospital of cases occurring while under treatment in the wards is 45.4 per cent. Dr. Osler estimated a possible recovery rate of 50 per cent., and Dr. Cushing of 50 to 60 per cent. We cannot but believe that a discriminating analysis in well-observed cases with complete pathological examinations would give a recovery rate considerably in excess of this, possibly 70 per cent.

PATHOLOGICAL CONSIDERATIONS. The *nature of the abdominal infection* in these cases is purely fortuitous, being drawn from the wealth of bacterial flora of the ileum, the possibilities of which have probably never yet been exhausted. The proportion of cases in which bacterial examination of the abdominal fluid has been made is very small, but such examinations have been more frequent in recent cases as their usefulness and prognostic value have become more evident. The infections as a rule, however, appear to be mild, largely bacillary, bacillus coli communis and bacillus mucosus capsulatus being the most

frequent. One strange incident of a pure infection of staphylococcus pyogenes aureus has been reported. Some half-dozen cases of infection with bacillus typhosus have been collected, from which it appears that these cases are attended with a high mortality. It will be necessary, however, to have a large number of cases in which a complete and careful bacterial examination has been made to give these results anything more than a passing interest. It is very desirable that our knowledge of the nature of these infections be widely increased, as it may eventually be found that certain features in the treatment can be altered to advantage according to the nature of the infection. It is possible that certain infections which are recognizable from cover-slip examinations will require very much less thorough irrigation, for instance, and that in some cases we are at present subjecting the patient to a considerably more severe strain than the circumstances may require. Cover-slips and cultures should be freely taken, and as these procedures require but a moment they need scarcely interfere with the rapidity of the operation. These examinations should be made not only from the fluid first encountered on opening the abdomen, but also from the lower and more dependent levels, as it sometimes happens that the upper part of the abdominal fluid appears to be free from organisms, and one is led to the erroneous conclusion that no bacterial infection has occurred. It is very desirable, also, to make an examination from the site of the perforation itself, and this, of course, is especially necessary in early cases where no appreciable amount of abdominal fluid is present.

It has been thoroughly demonstrated pathologically, and in several instances has apparently been clinically confirmed, that *infection of the peritoneal cavity may occur through the base of an ulcer without perforation*, or even through the inflamed portion of the intestine itself without deep ulceration. Such a case was reported by Dr. Ioison, " Du Traitement du Chirurgie de la Péritonite Suppurée Diffuse," *Revue de Chirurgie*, February 10, 1901, No. 2, where no solution in continuity of the bowel was found either at operation or autopsy. It is extremely probable, also, that such was the condition in the case of Dr. Dandridge, No. 28 of the Westcott series, in which no perforation was found, but the abdomen contained gas and free pus. The patient was irrigated and drained, and recovery followed. Such instances, however, are quite unusual, and it is hardly safe to assume that the case is of this variety, simply because no perforation is found in the rapid search of the ileum. It is, we feel, rather safer to assume that infection has occurred from some other source, which should be found and corrected as circumstances may permit.

It is probable that *adhesions* more or less extensive occur in all of these cases and that the infrequency with which they are reported is

due to inaccurate observation necessitated by a very restricted incision through which the bowel has been drawn before the examination was made. As mentioned above, this procedure does not seem wise, since adhesions forming a perfect protection for the peritoneal cavity against infection may be blindly broken up and the opportunity offered for general infection. It is not meant in recommending a rather more generous incision that there is a necessity for actual visual observation of the entire field, but that by this means sufficient care can be exercised in the withdrawal of intestine to prevent fecal extravasation and infection where such has not yet occurred. In cases of what appear to be sudden perforation it is doubtful if these adhesions are of sufficient consequence to afford much protection. In the Lakeside cases, while no adhesions were found in those operated upon for perforation itself, it was probably true that they were overlooked through insufficient care in the search for the lesion.

With reference to the *great practical value of complete postmortem examinations* in these cases, too much cannot be said. The greatest interest thus far seems to have centred in reporting certain clinical features and the circumstances of recovery, and from the small number and paucity of the postmortem examinations it is evident that very little interest has been taken in this part of the subject. It is perfectly useless to continue reporting simple recoveries for the sake of apparently increasing the recovery rate. What is most essential at the present time is a large collection of well-observed and well-reported autopsies. A complete examination, however, does not necessarily mean a complete autopsy. Through even a restricted incision it is possible to gain a fairly accurate conception of the extent and nature of the peritoneal infection if present; the appearance of the bowel for the sake of comparison with that observed at operation; the presence of additional perforations, overlooked or subsequent, and the existence of threatening perforations; the degree of success with which the suturing has been accomplished, and other respects in which the operative technique has been unsuccessful. Cultures may also be widely taken through such an incision, and the spleen, heart, and lungs examined. Blood cultures should also be taken. It is only in this way that we are going to be able to arrive at some definite conclusions as to the cause of death in these cases and the respects in which the treatment has been unsuccessful, and it is only by these means that the mistakes that are constantly being made in every case of perforation, either in diagnosis or treatment, can be rectified. For the sake of the present patients the clinical features and the operation are of sole consequence; the interest of future patients, for the present at least, lies almost entirely in pathological examinations.

In the apparent hope of giving some general direction to the clinical

features of these cases, Dr. Osler has published the specific instructions which are followed in the medical wards at the Johns Hopkins Hospital, " Perforation and Perforative Peritonitis in Typhoid Fever," *Philadelphia Medical Journal*, January 19, 1901, vol. vii. p. 116. This is as admirable a schedule as can well be imagined, and could most profitably be adopted for the sake of complete and uniform observation. To this schedule we would feel inclined, from an operative and pathological standpoint, to add certain suggestions which may be an aid in determining with more accuracy some of the unrecognized features mentioned in connection with these cases. Doubtful clinical features of so much consequence in establishing the all-important early diagnosis are covered by the Hopkins schedule. For the sake of a general and more accurate idea of the amount of systemic depression associated with the anæsthetic, the operation, or both, it is well to note with as minute accuracy as possible the condition of the patient immediately before and immediately following operation, as well as the changes in his condition for at least twenty-four hours subsequent to the operation. In taking cover-slips and cultures these should be obtained from various parts of the abdomen and also from the upper and lower portions of the abdominal fluid if present, and from the site of perforation. It is desirable to note with much care the general condition of the bowel, the nature and extent of adhesions, and the extent and severity of the general infection if present, for the sake of comparison with post-mortem examination in case the patient does not recover. In the post-mortem examinations, whether complete or restricted, the condition of the bowel and the extent of infection should be carefully noted; cover-slips and cultures should be widely taken from the abdomen, organs, and blood ; the condition of the operative field in the bowel should be carefully observed, also the presence of additional perforations, either those overlooked during the operation or those apparently subsequent to the operation, and the presence of threatening perforations. These are all points of special consequence, which, it is believed, will lead to an accumulation of facts of much practical value if carefully and generally observed. It is necessary to make so many of these post-mortem examinations without the direction of a trained pathologist that the circumstance seems to justify the mention of these details. It is from well-equipped hospitals that we must first look for such a class of reports, as elsewhere it is scarcely possible to have both medical and surgical observation of all typhoid cases, and especially of all suspicious cases. A means which will add very materially to the unity and usefulness of these observations and reports, and which will tend to develop a degree of judgment in diagnosis and operation that cannot possibly be obtained in any other way, may be afforded by having all these cases brought under the immediate control

of one member of the hospital staff. The number of perforations occurring during a year in any one institution is not large, and if the opportunities for observation and treatment are divided among a number of men the experience gained by each is very limited, the observations are very apt to be restricted and unmethodical, and the combined judgment rather biased and uncertain according to the nature of the particular case or two which has come to the hand of any one man. We feel that if this suggestion could be carried out our knowledge of this subject would be widely, rapidly, and very beneficially increased.

While, however, it is true that a large portion of these operations will still be done in hospitals, mainly on account of the difficulties in diagnosis, it is still interesting to note that there has been reported by a general practitioner one successful case in a country house under the conditions which one finds there ordinarily existent. The case was reported by Dr. R. T. Davis, "Perforation in Typhoid Fever; Operation; Recovery," *American Medicine*, January 18, 1902, vol. iii. p. 116. The operation was performed only six hours after perforation was thought to have occurred, which betokens a degree of watchfulness that one can scarcely hope to obtain with much frequency under such conditions. As this is the first case of its kind reported it is of special interest in showing the changing attitude of the medical profession in general with reference to perforation during the course of typhoid fever.

*12*

# CASE OF POSTTYPHOIDAL INFECTION OF A RIB.

## BY

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### of Cleveland, Ohio.

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Many cases of posttyphoidal infection of the ribs have been reported. Keen[1] published a list of 40 diseased ribs following typhoid. Horsley[2] has tabulated a list of 48 cases, and adds, that "Many reports are in such a fragmentary state that they cannot be used for tabulation."

The following case, occurring in the service of Dr. Dudley P. Allen at Lakeside Hospital, is presented with the hope that it may be of value in future tabulations. Dr. Henry S. Upson has kindly allowed me to use the medical history of the case.

N. F., a Hebrew, male, aged 37, married, was admitted August 23, 1902, complaining of headache, backache, and fever. His family history is good. His personal history shows he had pertussis and measles in childhood, and gonorrhea 13 years ago. Five years ago he was operated upon for fistula in ano. He had malarial fever 4 years ago.

His present illness began one week before admission. Previous to this time he was well. The initial symptoms were chills, sweats, headache, and general weakness, followed in 2 or 3 days by loss of appetite and inability to be about his usual work. On examination the patient was seen to be well-nourished. Mucous membrane was of good color. The tongue was dry and heavily coated. Pulse was regular, of fair volume, not dicrotic. Heart and lungs were negative. Abdomen soft, not tender. Spleen was not palpable. Several well-marked rose-spots were seen on the abdomen. Temperature was 104.6° F., pulse 90, respirations 25. The urine was amber colored, acid, specific gravity 1,022, no sugar, a trace of albumin, a few hyaline casts and leukocytes. No diazo reaction.

Examination of the blood was made at various times as follows:

    August 25: White blood count, 8,250. Widal negative.
    August 28: White blood count, 9,400. Widal negative.
    August 31: Test of patient's serum with the paracolon

[1] Surgical Complications and Sequels of Typhoid Fever.
[2] Annals of Surgery, February, 1903.

bacillus gave a negative result. Widal positive (1 to 10 and 1 to 50 dilution).

For a week from the time of admission the patient's temperature showed a daily variation between 102° to 104° F. During the second and third weeks there was a gradual decline of the temperature until the fourth week, when it became normal and continued so during the period of convalescence. The patient passed through an apparently uncomplicated course of typhoid fever and having gained rapidly in weight and strength was discharged October 11, 1902.

The subsequent history is as follows:

The patient said he experienced a slight pain in the region of the left lower ribs a few days after he left the hospital (October 11, 1902), and he noticed a slight swelling over the sternal end of the seventh rib.

About November 1, 1902, the swelling opened spontaneously and he came to the dispensary for treatment. The opening was enlarged and a small amount of pus evacuated. The patient continued to come to the dispensary for dressings. The wound, however, did not entirely heal, continuing to discharge considerably and causing severe pain at times.

On January 16, 1903, he was admitted to the surgical ward of the hospital. On examination a sinus, extending down to bone, was found on the sternal end of the seventh rib. Its opening was surrounded by a red, swollen area 3 cm. in diameter.

On January 20, under ether anesthesia, an incision 8 cm. in length was made over the sinus along the line of the seventh rib. About ½ dram of pus was obtained. The tract of the sinus was excised and the necrotic tissue about the rib, including some of the structure of the rib, was thoroughly cureted. The wound was packed with iodoform gauze.

In addition to this the patient also had an ischiorectal abscess, which was also incised and drained. Cultures from this abscess showed *Bacillus coli communis*.

The wound over the rib was repacked daily and continued to granulate. On February 3, 1903, 2 weeks after operation, the patient was referred to the dispensary for further dressings, as there was still a slight discharge from the wound.

## BACTERIOLOGIC REPORT.

A coverslip made from the smear showed a considerable amount of debris containing many pus cells, among which were a few small bacilli. A stain for tubercle bacilli was negative. Cultures were made upon the following media:

*Glycerin-agar.*—Whitish semitransparent growth upon the surface and a faint growth along the line of stab.

*Glucose-agar.*—A growth similar to that on glycerin-agar. No gas formation.

*Potato.*—The surface has a moist appearance but there is no visible growth.

*Milk.*—Slightly acid. No coagulation.

*Gelatin and Blood-serum.*—No liquefaction.

*Bouillon.*—A uniform cloudiness. Indol reaction negative. The bouillon culture was used in the agglutination test (2).

Coverslips from these cultures show a very actively motile bacillus varying in form, according to the medium on which it was developed, staining with the anilin dyes but not with Gram's stain.
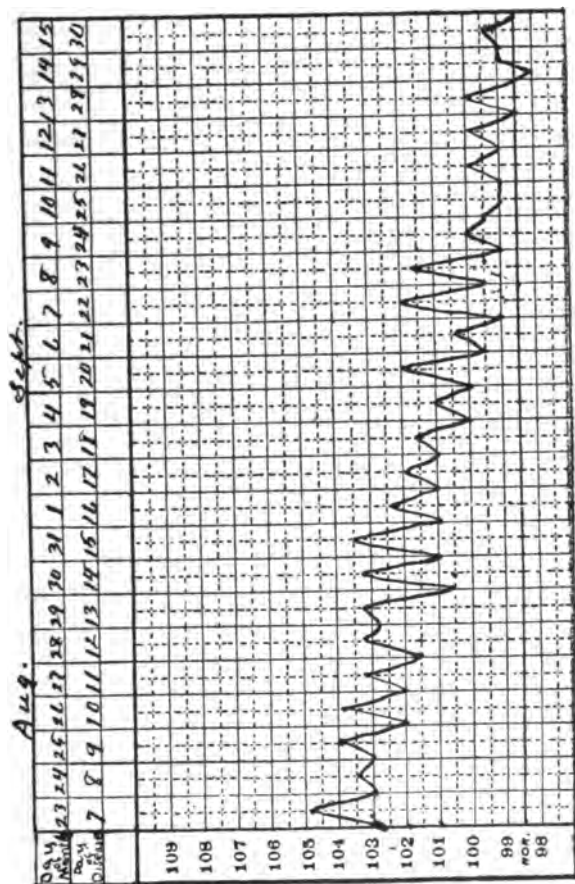
Typhoid Chart.

*Agglutination Tests.*—In all the tests a time limit of 1 hour was used and the test was not called positive unless there was good clumping and cessation of all motility. Serum was obtained from the patient February 16, 1903, and gave the following reactions:

1. With a known typhoid bacillus:

    1-10  Positive.................... ...................................... 10 minutes.
    1-50    "    ...................................................... .......45    "
    1-100 Negative—some motility after 12 hours.

2. With the bacillus above mentioned (bouillon culture 18 hours):

    1-10  Positive.......................................................... 5 minutes.
    1-50    "    ..................................................10    "
    1-100   "    ..................................................15    "
    1-200   "    ......... ................................... .......... .. 20    "
    1-300   "    ..................................................30    "
    1-500 Small clumps, but slight motility.
    1-750    "    "    "    "    "

3. Serum from a typhoid patient agglutinated the same bacillus (2) as follows:

    1-50  Positive...................................................15 minutes.
    1-100   "    ..................................................20    "
    1-200   "    ......... ..................................................25    "
    1-300   "    ..................................................45    "
    1-500 Small clumps, but still motile after 2 hours.

It will be seen by the foregoing that the organism is *Bacillus typhi abdominalis* or Eberth's bacillus.

### PATHOLOGIC REPORT.

The curetings were hardened in Orth's fluid and prepared by the celloidin method for microscopic study. The section shows a few bone trabeculas, the matrix of which takes a deep pink stain and contains numerous bone cells. One trabecula shows a light pink homogeneously staining matrix, within which are a few cartilage cells. The structure about the trabeculas is made up of a framework of connective tissue which, in some places, particularly between the marrow cells, is of a delicate type. The larger portion, however, appears as large bands of fibroblasts infiltrating and taking the place of the marrow tissue. Here and there are areas of marrow tissue showing cells of many varieties, including lymphocytes, plasma cells, mononuclear and polymorphonuclear eosinophiles, together with an occasional giant cell. Both the connective tissue bands and the marrow show a scattered, small, round-celled infiltration.

A few congested capillaries are seen in the marrow structure, also several large hemorrhagic areas which are probably due to traumatism. The remainder of the section is made up of granulation tissue, rich in newly formed and congested capillaries and showing large numbers of plasma cells, small round cells, a few eosinophiles, polymorphonuclear leukocytes, and red blood cells.

The process is evidently a chronic osteitis with the formation of chronic granulation tissue.

Stain for the bacillus in tissue: A section of the curetings was stained by the following method:
1. Stirling's gentian violet for 10 minutes.
2. Acetic acid, 1-1,000 for a few minutes.
3. Dehydrate in 95% alcohol.
4. Oil of cloves to clear.
5. Xylol.
6. Xylol balsam.

Microscopic examination of the section revealed a small, light-blue staining area near a small arteriole in one of the connective tissue bands. Within this area there were numerous deep-blue staining bacilli.

The foregoing data show conclusively that the case is one of a posttyphoidal infection of the rib producing a chronic osteitis with the formation of an abscess from which the typhoid bacillus was recovered in pure culture.

At the present writing, June 1, 1903, the patient still comes to the dispensary for dressings.

There are 2 small granulating areas over the junction of the seventh costal cartilage and sternum. There is still some discharge, and a small amount of induration in this region.

I am indebted to Dr. W. T. Howard, Jr., and Dr. L. W. Ladd, for reviews of this work.

# Wounds From Blank Cartridges

OBSERVATIONS UPON 16 CASES CARED FOR AT LAKESIDE HOSPITAL,
TOGETHER WITH A BACTERIOLOGIC REPORT

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About the fourth of July, of this year, a very unusual number of casualties were reported resulting from the firing of toy pistols. There was nothing unusual in the weapon itself, but the report made by the explosion of the cartridge seemed much louder than that which had formerly resulted from similar explosions. The shell of the cartridge itself is of brass. The nature of the explosive has not been determined. It seems, however, to possess unusual power. The number of injured patients who were brought to Lakeside Hospital suffering from wounds made by these blank cartridges was 15. There was one additional case of a wound of the hand by a sky-rocket. In the 15 mentioned injured by blank cartridges, the wounds were distributed as follows: There was one of the abdomen, one of the scrotum, one of the finger, and 13 of the hand. All of the wounds save one presented the same general characteristics. The wound of the abdomen was somewhat peculiar, and may, therefore, be described by itself. The patient, a boy of 10 years, was playing with a toy pistol. He had on trousers and a shirt. The explosion of the cartridge produced a wound on the left side of the abdomen. The external wound was small and seemingly superficial, and the boy did not seem to be seriously injured. I saw the boy on the morning of the fourth day following the injury. At that time there was a small wound the size of a slate pencil about three inches to the

left and a little above the level of the umbilicus. The abdomen was decidedly tympanitic, and there were evidences of peritonitis. A very grave prognosis was given, since it was evident that the peritonitis was already far advanced and the boy's condition was extremely serious. An anesthetic was administered and a small incision was made at the point of injury. It was found that the wound had penetrated the abdominal cavity, and that immediately behind it lay a coil of gut which had been so damaged that the integrity of its wall was destroyed. Immediately against the wall of the intestine was found the black wad of the cartridge. This wad had preserved its original form. The damage to the gut was so great that repair was impossible. The gut, therefore, had to be drawn into the wound, and an artificial anus was made. Notwithstanding what was done, the boy continued to fail, and died from general peritonitis the same day. This case has been reported first because it is unique, and also because it shows the explosive power and danger of these cartridges.

The wounds of the hand were almost all located in the palm. In all of them, so far as could be judged, the muzzle of the pistol must have been held close to the hand. The external injury was slight in most cases, consisting of a small irregular opening through the skin. On enlarging the wounds it was found that the channel broadened from the point of entrance, so that the wound in the interior of the hand was much larger than that of the integument. The wound extended, in some cases, almost the entire length of the hand, and in others penetrated the hand so that the wound passed from the palm of the hand upward between the metacarpal bones, and it was manifest that the back of the hand was involved in the injury.

The method of treatment pursued in the cases treated in the hospital was to anesthetize the patient, to lay the wound open thoroughly, to excise all lacerated and discolored tissue, to disinfect it with the utmost thoroughness, and to pack it open with iodoform gauze. In the majority of cases thus operated upon the wad of the cartridge was found intact in the deepest portion of the wound.

The cases treated in the hospital have been gathered under two heads, first, those which recovered without serious symptoms, and, second, those which died from tetanus. Omitting the case of wound to the abdomen, there were nine injured hands, which virtually received their primary treatment in the hospital. The wound of the injured finger alluded to above had been carefully washed, the opening packed with gauze, and had been repeatedly

soaked with carbolic acid before admission to the hospital, 12 days
after the injury. The treatment which the hands had received
previous to admission to the hospital had in all cases been super-
ficial dressings. In none of these nine cases had the wound been
opened or excised before admission to the hospital. The length
of time which the wound had existed before admission to the
hospital was as follows: Three had been injured less than 12
hours, six had been injured two days, and one had been injured
nine days. In addition to treatment by excision and packing with
iodoform gauze, as stated above, two cases, _viz._, one of my own
and one of Dr H. A. Becker, received prophylactic treatment by
the injection of serum. Every one of the 10 cases treated in the
hospital by the method described recovered.

The second class of cases were those which developed tetanus.
There were five of these. Four had injuries of the hand and
one had an injury of the scrotum. The previous treatment of
these cases had been as follows: In four of them an incision and
counter-opening had been made, how long after the receipt of the
wound it is impossible to say. In no case, however, had the
patient been anesthetized or the wound excised and cleared out.
The development of tetanus occurred in one case six days, in two
cases seven days, and in two cases eight days after the receipt of
the wound. All cases developed trismus and the deaths occurred
in from 12 hours to four days after admission to the hospital.
The treatment given in these cases was as follows: In all cases
the wounds were opened under ether and excised. All these
cases received treatment by intermuscular injection of antitetanic
serum. In one case antitetanic serum was injected, in addition,
into the lateral ventricles, through an opening made above them
in the skull. In addition to this the patients received antispas-
modics and anodynes to control the violence of the spasms, and to
some of them chloroform was administered to relieve the suffer-
ing. The case in which the injection of antitetanic serum was
made into the lateral ventricles of the brain lived for four days.
No other patient lived longer than 48 hours.

There is a two-fold reason for presenting this series of cases
to the Academy, the first is their professional interest, and the sec-
ond their public importance. The professional interest of the
cases depends upon various factors. The first of these factors is
that although the external wound caused by the wad of a toy
pistol is small, the injury to the deeper structures is much more
extensive than one would be led to anticipate from what appears
upon the surface. The wounds are relatively greater than those

which have resulted from the toy pistols heretofore, and are also far greater than those which are produced by the ball of an ordinary pistol.    Another factor of importance is that the serious symptoms in the cases did not develop at once.    The wound may remain quiescent for some days, presenting no conditions which would give rise to serious apprehension.    Later it becomes evident that there is deep inflammation, either upon the side of the hand which is wounded or upon the opposite side.    The appearance of serious symptoms on.the opposite side of the hand in several cases of tetanus treated in the hospital had resulted in counter-openings being made previous to their admission.    In none of the cases in which tetanus developed had anything further been done than to make counter-openings or to incise the original wound.    In no case had the original wound been cleared out and excised under an anesthetic.    The cases primarily operated upon in the hospital were, in all excepting a single instance, brought in the hospital within 48 hours after the injury.    The one which did not enter the hospital until the ninth day after injury was a case of a wound of the finger.    The wound had been cleaned out and packed with gauze although it had not been excised.

Although the number of cases is too few to permit of any positive conclusions as to the exact time after which it is impossible to avoid tetanus by excision of the injured tissues, the facts pointed out in these cases as to the length of time which the wound existed before treatment had been undertaken in those which recovered and in those which later developed tetanus, are most instructive.

The patients treated primarily in the hospital were generally cared for under the supervision of the resident surgeon, Dr Sanford, and to him largely is due the credit for the successful results obtained.    In all the cases treated primarily in the hospital the patients were anesthetized, the wounds were laid open, excised, thoroughly cleansed and packed open with iodoform gauze.    It seems, therefore, that this treatment must have been a large factor in the results obtained.    To what part of the treatment the success is due is, of course, a matter of uncertainty.    It may have been due to the thorough cleansing of the wound, but inasmuch as the bacillus of tetanus is an anerobic growth it seems that the success of the treatment may have been due to the fact that by packing the wounds thoroughly open there was a free access of air to every portion of the wound and, on this account, the pathogenic germ failed to develop.

With this idea in mind an attempt was made to gain some

added information by means of experiments conducted upon animals. These experiments have been carried on by the second resident surgeon, Dr Ludlow, and will be detailed in a paper which he will read this evening. Without anticipating what Dr Ludlow has to say in his paper, it is perhaps proper to state that the experiments have not been so successful in demonstrating the effect of treatment as had been anticipated. It is our intention to conduct these experiments further if it is found feasible to do so. Our idea in conducting the experiments was that if animals could be regularly inoculated with tetanus by shooting into them the wads from cartridges of toy pistols, it might be possible to demonstrate in a considerable series of cases that this development of tetanus could be avoided by certain treatment, viz., first by cleansing of the wound, second, thoroughly incising and excising it, and third, by packing it wide open with gauze and giving the air access to it. We have not, however, been successful in producing tetanus in animals by shooting them with the toy pistol.

There remains of course the open question in this connection as to whether the wad of the cartridge, the explosive of the cartridge, or the dirt which gained access to the wound at the time of or subsequent to the injury, is the source of infection. This also is a question which we have not thus far been able to solve.

The conclusions which it seems proper to record as the result of our observations are, first, that the cartridges of the present toy pistol are far more dangerous than those which were formerly used, and that the wound which is produced is far more extensive and more prone to produce tetanus. It seems also strongly probable from the fact that all cases treated primarily in the hospital by excision and open drainage recovered, that this treatment is one to be recommended highly, although it cannot yet be said that it is an absolute guarantee against the development of tetanus. The fact that five cases not so treated developed tetanus and that ten treated in this way did not develop tetanus is a strong recommendation for the treatment.

The vast amount of injury done by the toy pistol in Cleveland and in other cities of the United States, in July last, would seem to demand that scientific bodies, like our own, should point out in an authoritative way to the governing boards of our various cities that the manufacture and use of pistols of this kind should be absolutely prohibited.

CASES ENTERING HOSPITAL WITH TETANUS ALREADY DEVELOPED

| Name | Age | Injury | Date Injury | Entered Hospital | Previous Treatment | Condition on Entrance | Treatment | Result |
|---|---|---|---|---|---|---|---|---|
| C. C. | 26 | Blank Cart. Wound Hand. | 28 June | 30 June | Superficial dressing. Counter-opening dorsum. Wound not cleaned out | Trismus—Spasm neck muscles. | Serum { Intra-cranial. Intra-muscular Carbolic acid, Anodynes, Antispasmodics. Wound excised under ether | Death in 4 days. |
| B. S. | 8 | Blank Cart. Wound Scrotum. | 4 July | 10 July | Wound not cleaned out. | Trismus—Spasm neck muscles. | Wad removed from Scrotum. Serum—Antispasmodics. Anodynes. | Death in 12 hrs |
| N. G. | 18 | Blank Cart. Wound Hand. | 8 July | 11 July | Poultice to wound. Incision later. Wound not cleaned out. | Trismus.......... | Wound excised with ether Serum—Antispasmodics. Anodynes | Death in 14 hrs. |
| W. S. | 8 | Blank Cart. Wound Hand. | 4 July | 11 July | Wound incised with. Counter-opening, but not cleaned out. | Trismus—Spasm hand muscles. | Wound excised. Wad removed. Serum—Intra-muscular. Carbolic acid, Anti-spasmodics and Anodynes. | Death in 46 hrs. |
| F. M. | 13 | Blank Cart. Wound Hand. | 4 July | 12 July | Carbolic dressing with Incision of wound, but not cleaned out. | Trismus—Spasm neck and hand. | Wound excised with ether. Wad removed. Serum—Intra-muscular. Formalin (1:7000) infusion. Antispasmodics, Anodynes. | |

CASES PRIMARILY TREATED AT LAKESIDE

| Name | Age | Injury | Date of Injury | Date of Operation | Treatment | Result |
|---|---|---|---|---|---|---|
| W. M...... | 11 | Blank Cartridge wound, hand ..... | 4th July...... | 4th July (3 hours) | Anesthetized. Excision. Drainage. Iodoform gauze packing. | No symptoms thus far. |
| B. T...... | 22 | Lacerated hand (sky rocket)...... | 3rd July...... | 4th July (12 hours) | Ether. Excision. Drainage, etc...... | No symptoms thus far. |
| W. L...... | 24 | Blank Cartridge wound, hand .... | 2nd July...... | 4th July (2½ days) | Ether. Wad extracted Excision, etc *Prophylatic serum, 2 days. | No symptoms thus far. |
| W. W...... | 12 | Blank Cartridge wound, hand .... | 4th July...... | 4th July (1 hour) | Ether. Excision. Iodoform packing. | No symptoms thus far. |
| P. S...... | 28 | Blank Cartridge wound, hand .... | 3rd July...... | 5th July (42 hours) | Ether. Excision. Iodoform packing. | No symptoms thus far. |
| S. C...... | 8 | Blank Cartridge wound, hand .... | 4th July...... | 6th July (48 hours) | Ether. Excision. Iodoform packing. | No symptoms thus far. |
| A. O...... | 9 | Blank Cartridge wound, hand .... | 4th July...... | 6th July (48 hours) | Ether. Wad extracted. Excision. etc. | No symptoms thus far. |
| S. D...... | 37 | Blank Cartridge wound, hand .... | 4th July...... | 5th July (30 hours) | Ether. Excision. Drainage, etc. *Prophylatic serum, 5 days. | No symptoms thus far. |
| R. S...... | 11 | Blank Cartridge wound, hand .... | 4th July...... | 13th July (9 days) | Wound excised. | No symptoms thus far. |
| C. E...... | 10 | Blank Cartridge wound, abdomen . | 2nd July...... | 6th July (4 days) | Laparotomy. Colostomy. Lavage. | Death 6th July, from Gen'l Peritonitis. |
| A. B...... | 11 | Blank Cartridge wound, finger.... | 4th July...... | 16th July...... | Ether. Excision. Drainage, etc. | Outside treatment— Washed with carbolic and packed open— soaking repeatedly with carbolic. Wad was found in hand at Hospital. |

## BACTERIOLOGIC REPORT
### A. I. LUDLOW, M. D.

In accordance with our usual routine an effort was made to determine, as far as possible, the bacteriologic findings of the cases of blank cartridge-wounds.   Inasmuch as the tetanus bacillus developes only in the absence of oxygen it was necessary to make anerobic cultures.   When the wound was thoroughly opened, such part of the wad as was obtainable, together with the tissue in its immediate vicinity, was placed in a sterile test-tube and as soon as possible was transferred to the culture medium.

The cultures were made according to Wright's method. Two kinds of media were used, a 1% glucose bouillon and *agar agar*.   The medium fills the test-tube to a considerable height so that oxygen can less easily penetrate to the deeper portions.   The contents of the tube are boiled for a few minutes to expel the excess of oxygen from the medium.   The tube is then immersed in cold water to cool its contents rapidly, and then before the medium becomes solid, the tube is placed in a water bath at 38° C. for a few minutes.

When the medium may be assumed to have reached this temperature, it is inoculated with material from which the growth is to be obtained.   After the culture medium has been inoculated, the cotton stopper is thrust down almost to the medium and a second absorbent cotton stopper is inserted sufficiently far down into the test-tube so that the upper end is about one centimeter below the mouth of the tube.   Next there is run into the absorbent cotton stopper a small quantity of a watery solution of pyrogallic acid and about 1 c.c. of a 50% sodium hydrate solution.   The tube is immediately closed air tight by firmly inserting a rubber stopper sealed with wax or paraffin.

Cultures made in this way gave the following results:

1.   Cases which did not develop tetanus:

Five cases are included under this heading.   The cultures from three cases were sterile.   In the fourth case, *streptococcus pyogenes, staphylococcus pyogenes albus* and *bacillus mucosus capsulatus* were found.   The fifth case showed cultures of *strepococcus pyogenes* and *staphylococcus pyogenes albus*.

2.   Cultures from cases which developed tetanus:

In all of these cases symptoms of tetanus were apparent at the time the cultures were taken.

In the first case, the one on whom the intracranial injection was made, the culture was sterile.   In this case the wound had

been cleansed and soaked with bichlorid before the patient came to the hospital.

The culture from the second case showed a growth within 24 hours. After a week had elapsed, in order to give time for spore formation, the culture was examined. The medium presented a considerable amount of gas formation and a diffuse growth spreading out from the line of inoculation, particularly in the deeper portions.

Coverslips made from this culture showed many bacilli which were nonmotile. Some of these bacilli were straight or slightly curved with somewhat rounded ends and no spores. These bacilli were enclosed in a transparent capsule and stained by Gram's method, the *bacillus urogenes capsulatus*.

Many other bacilli were found appearing as slender, straight bacilli, with rounded ends. Some showed at the extremity of the bacillus a spore, spherical in form and considerably greater in diameter than the rods themselves, giving the bacilli the shape of a pin. This bacillus stained by Gram's method, thereby presenting both morphologically and in its staining properties the appearance of the bacillus of tetanus.

In addition to the above, arobic subcultures showed *streptococci* and the *bacillus mucosus capsulatus*.

From the third case the organisms were identical with those found in the second case with one important exception. In this case the bacillus which appeared almost identical with the tetanus bacillus, was more javelin shaped, decolorized by Gram's method and developed in the presence of oxygen. This was evidently the pseudotetanus organism.

More will be said later with reference to these cultures in animal inoculation.

The fourth and fifth cases showed the *bacillus mucosus capsulatus* and *bacillus arogenes capsulatus* but no organism like the tetanus organism could be found.

The startling feature in all these last four cultures was the large amount of gas formation, in one case it being so great as to force out the rubber cork.

### ANIMAL INOCULATIONS

Bouillon cultures from the second and third cases were heated to 80° C. for 20 minutes in an effort to destroy all but the suspected tetanus bacillus. One cubic centimeter of each solution was then injected subcutaneously into the hind leg of two guinea-pigs. A second anerobic culture made from the culture thus heated still showed both the tetanus bacillus and *bacillus arogenes capsulatus,* so both organisms were introduced at the inoculation.

Twenty-eight hours after inoculation the guinea-pig which had been inoculated from the culture containing the tetanus bacillus showed rigidity of the leg inoculated. Within six hours this leg showed tetanic contractions. The next morning the guinea-pig was found dead.        ●

At the seat of inoculation there was no suppuration. The internal organs appeared normal. Cultures were made from the tissues excised about the point of inoculation and showed *bacillus arogenes capsulatus* in pure culture. The tetanus bacillus could not be recovered. The *bacillus arogenes capsulatus* might therefore have had some part in the death of the guinea-pig.

The culture of *bacillus arogenes capsulatus* should have been injected into a guinea-pig but unfortu.nately this was not done. The guinea-pig inoculated from the culture containing the pseudotetanus and *bacillus arogenes capsulatus* was unaffected.

### SUMMARY

In the cases which did not develop tetanus the bacillus of tetanus was not found. In only one case of the five which developed tetanus was the tetanus bacillus found, and this organism was not recovered from the guinea-pig inoculated.

The finding of the *bacillus arogenes capsulatus* in four cases which developed tetanus is interesting. Has this organism anything to do with the phenomena assigned to tetanus? The action of light, especially sunlight, is very destructive to the tetanus bacillus. This suggests an experiment in regard to the action of the X-ray upon the growth of the tetanus. If it should prove destructive to the organism it might be of some value to submit the opened wounds to the X-ray treatment. The data in hand is too fragmentary to be of any value except as a suggestion for more work along this line of research.

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## THE EXTRAPERITONEAL RELATIONS OF THE APPENDIX VERMIFORMIS TO THE POSTERIOR SURFACE OF THE SECUM, WITH THE REPORT OF A FORM HITHERTO UNDESCRIBED.*

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THE case to which attention is invited in this article presents a very unusual and, so far as we can find, a unique anatomical placement of the vermiform appendix.

A girl of twenty years, a patient of Dr. I. N. Oakes, of North Ridgeville, Ohio, was referred for intercurrent appendectomy. The patient had suffered from three attacks of what appeared to be appendicular colic. The first attack was in June, 1903, and was manifest by nausea followed by pain in the right iliac fossa; the pain was not severe, and disappeared in two days; there was no fever. About a month later she had a similar attack, but even less severe. On August 20, she suffered a third attack, manifested by nausea, together with pain in the right iliac fossa, the pain being somewhat more severe than on the former occasions, and persisting for five days. On this occasion, as on the others, there was no fever, no chill and no vomiting, except once immediately after taking a dose of whisky. Turpentine stupes were applied in each instance. In none of the attacks was she confined to bed, although in the last attack she felt pretty miserable. These facts in the clinical history are mentioned, as they seemed to indicate the absence of a definite inflammatory condition. Since the last attack, however, there persisted a slight degree of sensitiveness on deep pressure in the region of the appendix. The patient lived in the country a considerable distance from ready communication, which fact, together with the manifest tendency toward increasingly severe recurrence, was the occasion for operative interference.

The operation was performed at Charity Hospital, Cleveland, October 21, 1903, and presented nothing of interest aside from the anatomical condition. The cecum and appendix were readily located, there being no adhesions. The appendix emerged from the cecum at the point noted in the large majority of cases, a little internal and slightly posterior to the projection of the caput, as in the classical third type of the cecum described by Treves.[1] Curving gently upon itself in a downward and backward direction, what appeared to be the tip of the appendix seemed attached to the cecum by an adhesion about 1.5 cm. below the appendiceal base. This at first appeared to be the entire appendix, and measured 2.5 cm. There was a mesoappendix arising from the under or left layer of the mesentery of the extreme distal portion of the ileum. The mesoappendix was about 2 cm. long at the base of the appendix, and was about 4 cm. along its free border, reaching what appeared to be the adherent tip of the appendix. This free border was nowhere attached to the parietal peritoneum, so that the apparently adherent tip of the appendix could be completely surounded by introducing the finger from the outer side underneath the appendix, beneath the mesoappendix, and out again below the free border of the mesoappendix.

The lack of any adhesions along this free border of the mesoappendix, in the presence of what appeared to be an adhesion of the tip of the appendix, was the first consideration that led to an understanding of the actual condition present. The end of the cecum was drawn upward, making prominent the line of reflection between the cecal and parietal peritoneum. On careful inspection it was now seen that what appeared to be the adherent tip of the appendix was merely a constriction narrowing the appendix to about one-fourth its proximal diameter. From this constriction the remainder of the appendix was seen in dim outline to lie extraperitoneally along the cecum as far as the line of peritoneal reflection mentioned, from which point it was lost to view in the retrocecal connective tissue. The extraperitoneal portion of the appendix was 1 cm. long. A short incision was made along the line of peritoneal reflection and the retrocecal

connective tissue separated along the appendix to its tip. This portion of the organ was 1 cm. long, making the entire appendix 4.5 cm. in length; the free mesenteric portion 2.5 cm., the extraperitoneal portion 1 cm., the retrocecal portion 1 cm.

The organ was readily removed. The mesenteric portion was 6 mm. in diameter, narrowing down at the constriction to a trifle over 2 mm.; beyond this point the diameter of the extraperitoneal and retrocecal portions widened out to 8 mm. The mucous membrane of the portion distal to the constriction was slightly congested, but this, together with the slight general thickening of the wall of the same portion, was the only gross evidence of inflammation. There were no adhesions. There were no foreign bodies. It is possible the distal thickening was due to muscular hypertrophy through efforts to expel mucus from this portion through the constriction. At all events the inflammation was slight and had not extended through the appendiceal wall.

That we have here a primary anatomical condition and not a condition resulting from inflammatory adhesions, there can be no reasonable doubt. An acute inflammatory condition gluing the appendix to the cecum would also have left the appendix adherent to the parietal peritoneum against which it rested posteriorly, which did not occur. An inflammatory process would undoubtedly have bound down the distal portion of the mesoappendix to the parietal surface against which it rested, but the distal border was not adherent and the finger could be freely run under it. If the extraperitoneal appearance of the middle portion of the appendix had been produced by recent adhesions, one would expect to find the remains of peritoneum on the cecal side of the appendix, but this portion of the organ was separated from the cecum only by loose connective tissue. Finally, no explanation along the line of inflammatory adhesions can possibly account for the location of the distal centimeter of the appendix lying in the retrocecal connective tissue.

The most frequent peritoneal relation of the appendix is where the entire organ lies freely in the peritoneal cavity supported by a mesoappendix extending only along the proximal half of

the organ, the distal portion being without a mesentery (Quain,[2] Sappey[3]) ; exception is taken to this statement by more recent investigators, notably Monks and Blake,[4] the opinion prevailing that the mesentery extends further along the appendix in a much larger proportion of cases than was formerly believed. An extraperitoneal relation of all or a part of the appendix is quite rare, except as the result of an inflammatory process.

Of 577 cases mentioned by Stroud,[5] only nine were partially or wholly extraperitoneal. Bryant[6] mentions three out of 144 cases examined by H. M. Biggs. Turner, quoted by Bryant,[6] found in 105 examinations four partially, and two wholly extraperitoneal. An examination of the records of 480 autopsies, performed in the Pathological Department of Lakeside Hospital, affords a series of 440 cases in which the vermiform appendix was free from gross inflammatory conditions or operative interference. Among these 440 cases only four instances appear in which any portion of the appendix was extraperitoneal, three of which occurred in the last few autopsies. Only one of these cases sustained a relation to the posterior surface of the cecum, as is mentioned later.

There have previously been recorded several types of extraperitoneal relations of the appendix to the posterior surface of the cecum and ascending colon, all of which are so well recognized that they merit no extensive reference list.

1. As the end of the cecum is drawn forward and upward, the appendix may be seen to be extraperitoneal, lying against the posterior surface of the cecum. There is, of course, no free mesentery. It is made possible only in the case of a short or much curved appendix, or where a considerable portion of the posterior cecal surface is covered by peritoneum, and the cecoparietal peritoneal fold is high up under the upper portion of the cecum or lower end of the ascending colon. (Deaver[7]).

2. A second form occurs when only the proximal portion of the appendix is in extraperitoneal relation to the posterior surface of .the cecum, while the distal portion to a varying degree projects freely into the peritoneal cavity, and is completely invested with the peritoneum. There may or may not be a short mesentery extending from

the cecum or ileum to this free distal part of the appendix. In such cases the distal portion may be thought at first to be the entire appendix, but it is noted that the longitudinal bands of the cecum converge on the real, not the apparent base of the appendix, and on careful inspection the remainder of the organ can be seen beneath the posterior peritoneal covering of the cecum. Such an instance is mentioned by Holmes,[8], and a figure given by Huntington.[9]

3. A third variety is seen where the proximal portion of the appendix is situated extraperitoneally against the posterior surface of the cecum, while the distal portion, instead of being free as in the second variety, passes upward along the posterior aspect of the cecum and ascending colon beyond the line of the cecoparietal peritoneal reflection, and lies in the connective tissue behind the large gut, entirely out of relation to the peritoneum (Huntington[10]).

4. Another relation exists when the cecoparietal peritoneal reflection is very low down, close to the tip of the cecum, so that the entire posterior surface of the cecum is extraperitoneal, and lies in direct contact with connective tissue. An appendix in this situation lies entirely in the retrocecal connective tissue, bearing no direct relation to the peritoneum (Huntington[11]).

5. A fifth variety, a modification of the third or fourth, is observed when the tip of the appendix, for a varying length, projects beyond the cecum on either side from the retrocecal connective tissue in which is buried all the remainder of the appendix, or at least its distal portion exclusive of the tip. The projecting tip is, of course, completely invested by peritoneum. Such an instance has been mentioned by Deaver,[12] and has also been recently observed by the writer.

6. Still another form is seen when the tip of the appendix lies behind the peritoneum against the posterior wall of the cecum, the proximal remainder being invested with peritoneum and supported by a mesentery that may be entirely free, or more or less adherent to the cecum. The extraperitoneal aspect may vary from what appears to be a mere adhesion, to a degre involving the entire distal half of the organ. In the first instance it resembles the case described by Treves,[13]

mentioned later, in which the tip was adherent to
the under surface of the mesentery of the ileum
instead of the posterior cecal surface. The other
extreme has been recently observed in the Path-
ological Department of Lakeside Hospital by Dr.
D. H. Dolly, resident pathologist, the entire distal
half of the appendix being extraperitoneal.

By reference to the description of the case
under consideration, it will at once be seen that
the situation of the appendix bears a certain rela-
tion to the third variety mentioned above. This
relationship, however, is confined entirely to the
distal half of the appendix, the first centimeter of
which lies extraperitoneally against the under
surface of the cecum, while the extreme centi-
meter or tip of the organ lies in the retrocecal
connective tissue above the cecoparietal peri-
toneal fold. The proximal half of the appendix
lies within the peritoneal cavity, and has an un-
adherent mesoappendix with a free margin, thus
resembling in a degree the sixth variety de-
scribed. It has been impossible for us to find,
after a careful independent search, any distinct
reference to a similar condition as an anatomical
entity, not the result of an inflammatory process.

The nearest suggestion we can find to the peri-
toneal relations existing in this case is a very gen-
eral statement given by Huntington,[14] in speak-
ing of the peritoneal relations of an appendix
which lies in the connective tissue behind the
cecum, he says, " Even in these cases, however,
the dorsal surface of the cecum and the root of
the appendix retain their free serous investment."
By reference to Fig. 517, described in this con-
nection, it seems apparent that the remark applies
to an appendix in which the root lies against the
cecum, and " the root of the appendix " has a
" free serous investment " as does the dorsal sur-
face of the cecum "; in other words, that the
outer or free side only of the appendix is covered
by peritoneum, the same layer covering the dorsal
surface of the cecum.

This brings the description under the third va-
riety mentioned above, from which reference
was made to Huntington. At all events it must
be observed that the text is not altogether clear,
that the reference is not specific, and that no
allusion is made to a free mesoappendix with an

unadherent distal margin. Treves[18] mentions a case in which the appendiceal tip was adherent to the under or left layer of the mesentery of the ileum forming a loop, but no reference is made to an extraperitoneal relation of any portion of the appendix.

It is instructive in this connection to consider certain embryological facts which may shed some light on this very unusual location of the appendix. Excellent figures illustrating these points may be found in the text of Huntington[15] or Kollman.[16] About the sixth week of the embryo the cecum develops as a bud on the posterior surface of the ascending limb of the umbilical loop. The twist toward the right of the posterior limb of this loop around the duodenocolic isthmus places the cecum in the right hypochondrium below the liver. This occurs about the fourth month, and the appendix at this time is already differentiated from the cecum by the overshadowing growth o fthe body of the latter. During the next three months, with but rare exceptions, the cecum gradually descends to the right iliac fossa, reaching this location about the seventh or eighth month. During the descent of the cecum with the formation of the ascending colon, the identity of the appendix is rapidly developed; a meso-appendix is doubtless present at a very early stage of this development

In most instances as the cecum descends, the mesentery of this portion of the gut becomes adherent to the dorsal parietal peritoneum of the abdominal cavity, and identical with it, the coalescence progressing from the median line outward toward the ascending colon and also from the above downward the peritoneal covering of the posterior part of the colon also unites with the dorsal parietal peritoneum, with which it comes in immediate contact, the two adherent layers eventually giving place to the retrocolic connective tissue. The failure of this peritoneal coalescence results in the unusual occurrence of a cecum and ascending colon, completely invested with peritoneum to a varying degree from below upward, with the presence of a longer or shorter mesentery from without inward toward the median line, according to the degree to which the coalescence has been deficient.

The retrocecal relations of the appendix appear to bear a relation to these embryological changes. While the explanations offered for the development of these relations are of necessity largely hypothecal, still it can be said of them that they appear to be logical and sufficient. As the cecum descends, it seems that the tip of the appendix occasionally becomes adherent to the posterior abdominal wall in the line of this descent. The peritoneal relations of the appendix produced in this way would vary according as the appendiceal tip became adherent high up or low down in the cecal course. Occurring high up, the cecal descent would carry the base down, eventually rendering the appendix taut. Still further descent would cause the cecum to overhang the base of the appendix to a varying degree, so that the appendix would appear to spring from the posterior cecal wall; this condition is also accentuated by the subsequent right lateral development of the cecum inferiorly. The descent progressing still further would eventually place the base of the appendix so far up on the posterior cecal wall that the coalescence of the cecal and parietal peritoneum with the formation of the retrocecal connective tissue would naturally reach below the base of the appendix, forming the ceco-parietal peritoneal fold at this point, and thus leaving the appendix lying completely in the retrocecal connective tissue and entirely out of relation with the peritoneum. This is the condition met with in the fourth variety mentioned above.

Having these changes in mind, it is readily conceivable how some of the other relations of the appendix previously described may occur. The appendix becoming adherent lower down, or the descent of the cecum being less marked, only the distal portion of the appendix may come to lie in the retrocecal connective tissue, while the remaining proximal portion, merely being drawn snugly against the lower part of the cecum, still lies in relation to the peritoneum. The peritoneal surface of this proximal portion now lying in contact with the peritoneum of the posterior cecal wall coalesces with the latter and changes to connective tissue precisely as in the case of the cecum and parietal peritoneum, so that eventually

the proximal portion is covered by peritoneum on only one side, while the distal portion lies above the cecoparietal fold in the retrocecal connective tissue. The mesoappendix also becomes adherent to the cecum; and it is sometimes thought to be traced as a thickened peritoneal surface on the cecum to the inner side of the adherent proximal portion of the appendix. In this way is explained the third form previously mentioned.

For an explanation of the case under special consideration we must naturally turn to changes produced in this same line of development, since it bears such a close and suggestive relation to the third form, the development of which we have just considered. It seems most probable that in the case reported the tip of the appendix became adherent rather late in the descent of the cecum so that only a small portion, 1 cm., became lodged in the retrocecal connective tissue. It would seem that this condition eventuated when the cecum had nearly reached its lowest position and the appendix, instead of being drawn taut against the cecum, still had a considerable proximal portion free in the peritoneal cavity with a mesoappendix extending 2.5 cm. outward from its base. The portion of the appendix between the retrocecal tip and the mesenteric portion, a distance of 1 cm., became adherent in some way to the cecum, the adherent peritoneal surface changing to connective tissue.

That this process of adhesion of the appendix to the cecum should have stopped exactly at the point where the mesoappendix ceased, leaving the distal edge of the mesoappendix entirely free and the proximal 2.5 cm. of the appendix in the usual relation to its mesentery, is strange and very unusual, but entirely conceivable in the order of development. Had the distal edge of the mesoappendix become adherent, a fossa would have been formed extending under the free portion of the appendix and the remainder of the mesoappendix. This fossa might later have been entirely obliterated by adhesion of the mesoappendix to the cecum, the free portion of the appendix also becoming adherent, and thus produced a condition quite similar to that described under the development of the third form, though brought about in a different way.

Aside from its anatomical interest, this very unusual relation of the appendix possesses two elements of clinical interest. The unavoidable presence of a bend or kink in the appendix at the termination of its mesenteric portion has, of course, the same significance as a similar condition existing under other circumstances, the importance of which has been so admirably insisted upon by Allen.[17] The other clinical feature is the possibility of an intestinal obstruction owing to the insinuation of a nuckle of small gut under the free mesenteric portion of the appendix, beneath the mesoappendix, and out below its unadherent distal margin; such a possibility was noted by Treves[13] in the case showing a free appendiceal loop, to which reference has been made.

Although adding nothing to the present discussion, a contribution by Peronidi[18] gives an extensive bibliography on the anatomy of the cecum and appendix, containing many articles to which reference would otherwise have been made in the paper.

### REFERENCES.

1 Treves, F. The Anatomy of the Intestinal Canal and Peritoneum in Man, p. 34 (1885).

2 Quain's Anatomy, Vol. III, Pt. IV, p. 109 (1898).

3 Sappey, P. C. Traité d'Anatomie Descriptive, T. IV, p. 224 (1889).

4 Monks, G. H., and Blake, J. B. The Normal Appendix; its Length, its Mesentery, and its Position or Direction, as Observed in 656 Autopsies. *Boston Medical and Surgical Journal,* Vol. CXLVII, p. 581, Nov. 27, 1902.

5 Stroud, B. B. Notes on the Appendix (Abstract), Proceedings of the Tenth Annual Session of the Association of American Anatomists, Dec. 28, 1897, p. 127 (1898).

6 Bryant, J. D. The Relations of the Gross Anatomy of the Vermiform Appendix to Some Features of Clinical History of Appendicitis, *Annals of Surgery,* Vol. 17, p. 164 (1893).

7 Deaver, J. B. A Treatise on Appendicitis, p. 34, Pl. V (1900).

8 Holmes, E. W. The Appendix Vermiformis, *The Pennsylvania Medical Journal,* Vol. 31, p. 205, Jan., 1902.

9 Huntington, G. S. The Anatomy of the Human Peritoneum and Abdominal Cavity, p. 276, Fig. 574 (1903).

10 Huntington, G. S. Loc. cit. p. 241, Fig. 517.

11 Huntington, G. S. Loc. cit. p. 258, Fig. 558.

12 Deaver, J. B. Surgical Anatomy, Vol. III, p. 174, Pl. 342 (1903).

13 Treves, F. Loc. cit. p. 44.

14 Huntington, G. S. Loc. cit., p. 251.

15 Huntington, G. S. Loc. cit., p. 237.

16 Kollman, J. Lehrbuch der Entwickelungsgeschichte des Menschen, p. 375 (1898).

17 Allen, D. P. The Origin of Appendicitis. Transactions of the American Surgical Association, Vol. XV, p. 561 (1897).

18 Peronidi, G. Recherches Anatomiques sur le Cæcum et son Appendice. *Revue de Chirurgie,* T. XXII, p. 221, August, 1900.

# LUMBAR ABSCESS;

## REPORT OF SIX CASES TREATED BY ASPIRATION AND IN-JECTION OF IODOFORM-GLYCERIN EMULSION.

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No attempt is made, in this report, to establish the absolute value of aspiration and injection of lumbar abscess with the iodoform and glycerin emulsion. The investigations already made in regard to this method show that it is of great benefit to many patients. Although the cases cited below are too few in number to be of positive value in themselves, yet when added to other reported cases they may be of some confirmatory value. It is with this idea that we present the following cases, occurring in the service of Dr. Dudley P. Allen at Lakeside Hospital.

CASE 1.—A male, aged 25 years, white, single, admitted to the hospital Feb. 7, 1898. Four months previous to the time of entrance the patient noticed a swelling about the size of a walnut in the right inguinal region. The tumor gradually increased in size, but at no time did it cause pain.

*Family History.*—Father, mother, four brothers and one sister living and well. One sister died of pulmonary tuberculosis at the age of twenty-three (six years ago).

*Personal History.*—Measles during childhood. For the last three years, particularly in winter time, he has been troubled with a cough. His physician told him that he had pulmonary tuberculosis. In April, 1898, the patient complained of severe pain in the right lumbar region. This lasted about three weeks, during which time he experienced some fulness in the right groin whenever he flexed his right thigh on his abdomen. After this period, however, no symptoms were noticed until the distinct swelling appeared.

*Physical Examination.*—The tumor is somewhat pyriform in shape, about one-half larger than the ordinary incandescent lamp, and extends from the right external abdominal ring upward, backward and outward, just above Poupart's ligament

along the crest of the ilium to the midaxillary line. The tumor is fluctuant. The skin is normal in color and there is no increase in surface temperature. The remainder of the physical examination is negative except for some dulness in the right supraclavicular and infraclavicular spaces.

*Treatment.*—The patient received no treatment before coming to the hospital. In this, as in the following cases, the operative treatment consisted of a thorough sterilization of the skin over and about the tumor, followed by aspiration of its contents with a trocar. As a rule, about three ounces of an emulsion of iodoform and glycerin, fifteen grains to the ounce, were injected into the abscess cavity. In the majority of cases the operation can be done under local anesthesia. In this case ten aspirations and injections were made. The first two at intervals of a week and the remaining eight at intervals of two weeks. During the periods between the last eight aspirations the patient was permitted to return to his home. At each aspiration, except the last, from six to ten ounces of fluid were withdrawn, the first being of a whitish color, containing a cheesy material, while the remainder were of a dark brown color. At the last aspiration only one ounce of a reddish brown fluid was obtained.

*Results.*—The bacteriologic findings werd negative, all cultures being sterile. The patient has been seen within the last few days and shows no evidence of return of the abscess. It might be interesting to add that in February, 1901, while he was troubled with a severe cough, tubercle bacilli were found in his sputum. At present, October 21, 1903, however, he is gaining in weight, has had no cough for many months, and seems to be in excellent condition.

CASE 2.—This patient, a female, aged 19, white, single, was admitted to the hospital April 15, 1899.

*Family History.*—Negative.

*Personal History.*—General health good except for the present trouble. She gives a history of three injuries to her back, but does not remember the time or location of the injuries.

A year previous to admission the patient began to have pain in the lumbar region, especially when arising from a chair or after jarring the body by a misstep. The pain and discomfort gradually increased. In October, 1898, she was advised by her physician to try absolute rest. Accordingly she remained in bed for three months, which resulted in marked improvement. In February, 1899, she noticed a swelling just above Poupart's ligament on the right side. A smaller swelling, together with a general fulness more externally, appeared just to the left of the vertebral column in the lumbar region.

*Physical Examination.*—This was negative except for the swelling above noted.

*Treatment.*—April 19, 1899, twenty-five ounces of light green cloudy pus were removed from the left lumbar region, the trocar being inserted near the apex of Petit's triangle. Although only two ounces of the emulsion were injected, the urine, on the next day, gave a strong iodin reaction.

On May 2 the right inguinal tumor was aspirated, and five ounces of greenish pus obtained. The same amount of emulsion was used, but the urine gave no iodin reaction. Ten days later the trocar was inserted in the left inguinal region where a swelling had appeared and four ounces of grayish pus were withdrawn.

One week later this same region was again aspirated and three ounces of grayish pus removed. A month intervened before the next aspiration. During this period the patient was out of doors in a wheel chair every pleasant day.

At the last aspiration, on the left side, about five ounces of greenish pus were evacuated.

Cultures made at the time of each aspiration were sterile.

*Results.*—Three months after this last aspiration the patient was examined by Dr. Allen and no indication of any reaccumulation could be detected. At the present time her physician says that there has been no reappearance of the abscess and that her general health is excellent.

CASE 3.—Female, aged ten years, white. Admitted to the hospital Feb. 7, 1901.

*Family History.*—Father died of tuberculosis at the age of 35. Mother died of the same disease at the age of 30.

*Personal History.*—Patient fell down stairs when one year old. No trouble was apparent until a year later, when the spine showed some kyphosis in the lumbar region. Since this time she has suffered repeated attacks of pain in the back at various times. About a year ago (November, 1899) she began to complain of pain in the left knee. Frequently the pain has been so severe as to cause her to remain in bed while in the intervals between these attacks she could play and walk about as usual. One month ago the pain became especially severe, and since that time it has been almost constant. In addition to this trouble she gives a history of pertussis, measles, scarlet fever, varicella and diphtheria. She has coughed considerably from time to time for the last four years.

*Physical Examination.*—The heart was found normal. The lungs show a few râles at the right apex, posteriorly, and râles over the larger portion of the left lower lobe. The lumbar vertebræ show a marked kyphosis and the dorsal vertebræ a mild scoliosis. Examination of the extremities negative, except that percussion of the left lower extremity in its axis causes mild pain in the hip.

*Treatment.*—The first treatment employed was rest in bed

and constitutional treatment. Extension was applied for two weeks, giving considerable relief. On April 1, 1901, a swelling was noticed in the left inguinal region. It began to increase in size and became tender. The next day a trocar was inserted 3 centimeters above the left anterior superior spinous process of the ilium and several ounces of thick yellow pus aspirated. The usual amount of emulsion was injected into the cavity. Two weeks later, the abscess having reaccumulated, the same process was employed. For a few days the patient was somewhat depressed, and iodin was demonstrated in the urine.

*Results.*—Within a week, however, she commenced to improve greatly, and on June 1 she was placed on a Bradford frame. As often as the weather permitted she was taken out of doors. Under this treatment she gained rapidly in weight and strength. There was no evidence of reaccumulation of the abscess when the patient was discharged. At the present time (October, 1903) there is still no indication of return of the abscess. Her general health is good and she is able to attend school regularly.

CASE 4.—Female, aged 39 years, white, single, was admitted to the hospital Jan. 31, 1902.

*Family History.*—Negative.

*Personal History.*—She had typhoid fever three years ago, but otherwise her general health had been good until July, 1900, when she began to have "neuralgic" pains in her right hip and thigh. Later the corresponding parts on the other side of the body were affected. From the time of the first attack the pain has been fairly constant, being aggravated after exertion. She experienced difficulty in rising up after stooping down to pick up objects from the floor and often was obliged to assist herself by taking hold of a chair or table.

In December, 1901, she noticed a mass just above the left iliac crest, anteriorly, which has gradually increased in size and has caused her to favor that side in walking. She has never had any symptoms localized in her back at the site of the kyphosis.

*Physical Examination.*—The heart and lungs are normal. At the second and third lumbar spines there is a kyphosis slight in degree, but distinct. A mass can be made out in the left iliac region extending about half way from the anterior superior spinous process of the ilium toward the median line, downward toward the pubes and upward to a little above the crest of the ilium. It is distinctly fluctuant, and the amount of tissue covering it anteriorly is evidently not great.

*Treatment.*—Previous to entering the hospital she had received no treatment. After rest in bed for a week, the left iliac region was aspirated in the usual manner, the trocar being inserted just above and to the inner side of the left

anterior superior spine of the ilium. Sixteen ounces of greenish pus were drawn off and three ounces of the iodoform emulsion injected. Within a week the abscess cavity began to refill, and February 24 a second aspiration was made at which time the same amount of pus was removed. During the interval between this and the next aspiration the patient was up in a wheel chair almost every day. March 19 it was evident that another aspiration was necessary, for distinct swelling and fluctuation could be made out in the left iliac region. Accordingly, this was done, and again sixteen ounces of greenish pus were evacuated. A week after this aspiration the patient was allowed to return home after being instructed to live out of doors as much as possible. On April 21 she returned to the' hospital. The abscess had reappeared and distinct fluctuation was present. The next day the abscess was again aspirated and this time about eight ounces of yellowish pus were obtained.

*Bacteriologic Report.*—The coverslip and cultures from the pus obtained at the first aspiration were negative. Pus from the second aspiration showed the presence of the *Bacillus proteus vulgaris.* Cultures from the third and fourth aspirations were sterile. No tubercular bacilli could be detected.

*Results.*—The patient was allowed to go home after the fourth aspiration with instructions to report from time to time. She was seen by Dr. Allen June 27, 1902. Her general health was very much improved and she felt much stronger, although she had not gained much in weight. A little thickening was made out in the iliac fossa, but no fluctuation could be perceived. The patient was again examined in December, 1902. There was no evidence of return of the abscess. Her general health was excellent. At the present time (October, 1903) there is no return of the abscess.

CASE 5.—Female, aged 7 years, was admitted to the hospital Jan. 2, 1903.

*Family History.*—Father, mother, two sisters and three brothers are living and in good health. Her grandmother and uncle died of pulmonary tuberculosis.

*Personal History.*—The patient's general health has been fairly good. About two years ago her parents noticed a bulging of the spine. Until six months ago the patient complained of no pain, but at that time she commenced to limp and suffer pain in the left knee. The kyphosis has been gradually increasing to the present time.

*Physical Examination.*—There is a marked kyphosis with a slight right scoliosis beginning at the eleventh dorsal vertebra and extending to the fourth lumbar. There is no tenderness on pressure. Some resistance can be made out in the left iliac fossa. The remainder of the physical examination is normal.

*Treatment.*—Three days after admission to the hospital a plaster jacket was applied, and three days later the patient was allowed to go home.

June 18, 1903, the patient returned to the hospital with a large fluctuating mass on the upper and outer side of the left thigh. This mass has been gradually increasing in size for the past few weeks. It was unattended with pain or redness. The day after admission, under ether anesthesia, the abscess was evacuated and 325 c.c. of thick dirty yellow pus removed. The usual amount of iodoform emulsion was injected. The next day iodin was found in the urine. June 29, the abscess having reappeared, it was again aspirated, and this time 300 c.c. of pus were removed. A third aspiration was done on July 7, at which time about 300 c.c. of yellowish fluid were obtained. July 24 a fourth aspiration was made and eight ounces of brownish fluid were withdrawn. This time four ounces of the emulsion were injected. Two days after the aspiration there was the only marked rise of temperature during the course of the aspirations. On this day the temperature was 102 F.

*Bacteriologic Report.*—Cultures taken at the time of each aspiration were sterile.

*Results.*—July 29 the thigh appeared practically normal, so the patient was sent home with instructions to her physician to send her back to the hospital if the abscess reappeared. Up to the present time (October, 1903) there has been no return of the abscess, and the patient is in excellent health.

CASE 6.—A female, aged 33, white, married, was admitted to the hospital Aug. 6, 1903.

*Family History.*—One sister died of tuberculosis.

*Personal History.*—Patient had diphtheria two years ago. She has always been of a nervous disposition. Five years ago she had an attack of pain in the lumbar region. At that time she thought the trouble must be rheumatism. These attacks of pain continued to come on at varying intervals. Between the attacks she was fairly well, although she had some difficulty in arising from a reclining position or on attempting to pick up any object from the floor. At night this pain was so severe that she would cry out. About ten months ago a swelling appeared in the right inguinal region.

*Physical Examination.*—In the region of the lumbar vertebræ there is a well-marked scoliosis to the left and a well-defined kyphosis in the same region. In the right groin there is a swelling about three centimeters in diameter, fluctuant and becoming smaller when the patient reclines. The remainder of the physical examination is negative.

*Treatment.*—Aug. 8, 1903, under local anesthesia, an aspirating needle was inserted into the tumor mass and 300 c.c.

of greenish yellow pus removed. Two ounces of the iodoform emulsion were injected. The day after the operation the urine gave a reaction for iodin. A second aspiration was made August 13 and eight ounces of yellowish serous fluid withdrawn. One week later very little swelling could be detected and by August 30 the mass had entirely disappeared. On August 31 the iodin reaction disappeared from the urine. The patient was sent home on a cot with instructions to remain in bed several weeks.

*Bacteriologic Examination.*—The pus contained many leucocytes, but both cultures were sterile.

*Results.*—At present the physician who is attending the patient reports that he has detected no return of the abscess.

### SUMMARY.

1. Four cases gave a family history of tuberculosis.

2. Five cases occurred in females whose ages ranged from 7 to 39 years and one case in a male 25 years old.

3. Two patients gave a history of injury to the back.

4. In three cases two aspirations were made, in one case three, in another four, and in another ten.

5. The urine from four cases out of the six gave a reaction for iodin the next day after the aspiration. This reaction persisted only for two or three days, except in one case in which it persisted for two weeks.

6. Slight mental depression was noticed in two cases.

7. As a general rule, there was an elevation of temperature from two to four degrees following each aspiration.

8. The cultures were sterile in every case except one, in which the *Bacillus proteus vulgaris* was obtained.

9. In all the six cases there has been no indication of return of the abscess after a period of five years in one case, three years in another and two years in a third, while in the remaining three one year or less has elapsed since the last aspiration. There was a marked improvement in the general health of

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# A CLINICAL AND PATHOLOGICAL REPORT OF A CASE OF SPLENIC ANÆMIA.

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AND

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1. Clinical Report (Dr. Sanford). *Case of anæmia of long duration with gastrointestinal disturbances and pain in splenic region; recent severe and repeated hemorrhages by stool and vomitus following traumata; blood characteristic of secondary anæmia of chlorotic type without leukocytosis, with no general lymphatic enlargement; idiopathic splenomegaly; exploratory laparotomy; subsequent splenectomy; death.* Mr. B. R. T., aged twenty-eight years, married, a farmer, of Greenwich, Ohio, was sent to Lakeside Hospital on the evening of October 14, 1903, with symptoms of vomiting of blood, tarry stools, profound anæmia and a tumor in the lower mid-abdomen.

The patient stated that three weeks before he had been thrown over the head of a spirited horse and had struck flat on his back, but had not been prevented from working about as usual. Two weeks later, which was a week before entrance, he was jerked off his feet and thrown violently some distance by this same horse which he was leading. The following morning he had a copious black liquid stool, after which he vomited much blood, he thinks at least a pint, of both dark blood clots and some fresh blood. This vomiting continued at intervals that day, and then stopped, but he had large tarry stools nearly every day up to the time of his entrance. He was in bed during most of the time, felt greatly prostrated, and had no appetite.

His physician on the day before he was brought to the hospital first noticed a tumor in the lower mid-abdomen, which he took to be a distended bladder, but on catheterization its size was not altered. The urine appeared normal and contained no blood. Dr. Maynard, of Elyria, who was called in consultation, then sent him to the hospital. On entrance the patient seemed greatly fatigued from his journey and could answer questions with difficulty.

*Physical Examination.*  Patient is a young American, slight in
frame, very sallow, somewhat emaciated, in considerable state of
shock.  Temperature, 100.6°; pulse, 120, small volume, regular,
compressible; respiration, 28.

Sclera subicteric; teeth poor; tongue furred and moist.

Chest, slender and shallow, expansion equal and good; clavicles
and ribs prominent; supraclavicular and infraclavicular fossæ deep;
no glands palpable.  Interspaces sunken; epigastric angle narrow.

Percussion note dull over clavicles and supraclavicular spaces,
elsewhere hyperresonant.  Breath sounds clear front and back;
musical rales on expiration in left foreaxillary line.

The area of cardiac dulness is hard to define; it apparently
extends somewhat to the right of the sternum; a blowing systolic
murmur is heard all over the base, and not at the apex or in the
axilla.

The abdomen is sunken, scaphoid in general outline, somewhat
sensitive to palpation in the left upper quadrant where there is
slight muscular rigidity.  Liver dulness begins at the fifth space
in nipple line and extends to costal margin.  Splenic dulness not
made out.  The pole of right kidney is palpable on deep inspiration.
Left kidney not felt, and it seems with one hand in the left lumbar
region and the other under the left costal margin that the two hands
can be brought nearer together with less intervening structures on
the left than on the right side.  On pressure here the patient is
evidently sensitive, although apathetic to examination elsewhere.
Just below the umbilicus is a mass, oval in general outline, lying
diagonally, its higher pole to the right, smooth, hard, not tender,
quite freely movable, edges rounded, no notches felt.  The abdomen
is everywhere tympanitic except over the mass described where the
note is flat.

The inguinal glands are slightly enlarged.  Rectum empty except
for a few small clots; no hemorrhoids; extremities thin; no tibial
scars or œdema.

The patient was given artificial heat and stimulation by strychnine
and saline subcutaneous infusions every six hours.  Milk and whites
of eggs; morphine for restlessness.  A glycerin enema resulted in
a black liquid stool, which on examination was found to be largely
decomposed blood.

The immediate history of severe repeated traumatisms combined
with the patient's statement that he had always been well previously,
quite naturally led one to regard the present symptoms as the direct
result of the injury rather than to seek a more remote cause.  Various
possibilities were considered, among which hemorrhage from a
gastric or duodenal ulcer, and a dislocated viscus were foremost.
Neither diagnosis seemed to account for all the symptoms, and in
view of the later developments in the case, a further discussion of
these points is unnecessary.

The patient reacted fairly well to stimulation, and was kept under observation the next day, during which he had seven more black liquid stools. Rectal feeding was added to the treatment which was otherwise the same.

A blood examination on the day after admission showed: Reds, 2,800,000; leukocytes, 8000; hæmoglobin, 25 per cent.; coagulation time 45 seconds; no plasmodia seen.

The next day the patient's unchanged condition and the uncertain diagnosis seemed to warrant an exploratory operation which was decided upon.

*Operation, October 16th* (Dr. Dudley P. Allen. Gas and ether). *Laparotomy; exploration.* An incision 9 cm. in length was made in the median line below the umbilicus and over the tumor. A small quantity of clear peritoneal fluid was met with from which cultures were taken. The intestines were normal. The mass was identified as the spleen, greatly enlarged and displaced, freely movable, otherwise of normal appearance. Accurate measurements were not taken, but the organ seemed at least two or three times its normal size. The surgeon considered any operative procedure on the spleen unwise in the patient's condition and closed the incision. Another incision in the median line of the epigastrium was then made and the stomach inspected, and found normal. Nothing abnormal felt about the liver, gall-bladder, appendix, or pancreas. Palpation of the kidneys showed them apparently normal in position and size. The incisions were then closed. The patient received very little shock from the operation, which took but fifteen minutes.

The conditions found at operation raised the question whether the traumata might not be coincidences or, perhaps, exciting causes in producing the appearance of symptoms primarily due to some as yet unrecognized organic lesion. The arrival of the patient's friends gave the first opportunity of getting the family and previous history in the case, which was as follows:

*Family History.* Father died of "broken back" at the age of seventy years. Mother and one brother living and well. An uncle died of heart disease. No history of malaria, syphilis, cancer or tuberculosis in the family.

*Previous History.* Patient had children's diseases. He has always been pale since childhood. Between seven and eight years ago he had an attack of very violent vomiting which continued all night and was not connected with any indiscretion in diet; vomitus contained no blood. He has always had poor digestion, often distressed after meals, sometimes vomiting, with relief to the discomfort.

In the summer of 1902 he had "bowel trouble," in which there was diarrhœa, griping pains, severe vomiting, with some blood in stools and vomitus. From this time up to the injury the patient was not well, and was under a doctor's care for general "ill feeling"

and frequent urination. In the winter of 1902, he also complained
of a good deal of dragging pain in the back and left side. No
history of venereal disease; tobacco in moderation; no alcohol.
Patient has not lived in a malarial district and never had periodic
chills.

With this suggestive history and the enlarged and dislocated spleen
found at operation, a detailed blood examination was then made
and showed the following conditions: Reds, 3,480,000; leukocytes,
8500; hæmoglobin, 25 per cent. Differential count of 600 cells:
polymorphonuclears, 74 per cent.; small mononuclears, 18 per cent.;
large mononuclears, 4 per cent.; transitional forms, 1.5 per cent.;
eosinophiles, 2.5 per cent. Red cells took stain poorly, and were
variable in shape and size, centre quite thin, no rouleau formation,
some poikilocytosis, six nucleated reds seen; no plasmodia.

The urine was amber, clear, specific gravity, 1020, acid, no sugar,
faint trace of albumin, sediment, few leukocytes, epithelial cells.

The case then presented the following data: A patient with
(1) a previous history of an anæmic condition with gastrointestinal
disturbances and pain in the splenic region; (2) an immediate
history of severe and repeated hemorrhages by stool and vomitus
following traumatism; (3) a present condition of profound anæmia,
with the blood characteristic of a secondary anæmia of the chlorotic
type without leukocytosis, with no general lymphatic enlargement;
and (4) a splenomegaly apparently not due to malaria, syphilis,
tuberculosis, leukæmia, or amyloid disease. From this symptom-
complex the possibility of the existence of splenic anæmia was
strongly suggested and a course of supporting treatment was
instituted while further study could be carried on.

During the week after operation the patient's general condition
improved slightly. The stools no longer contained fresh blood,
but were dark, copious, watery, varied between three and seven
daily and were at times involuntary. There was no further vomiting.
Liquid nourishment was well taken. The temperature ranged
between 99.5° and 101.5°, and the pulse from 100 to 140. The
outline of the tumor was marked out on the abdomen in silver
nitrate solution to watch for changes in its size or position.

On the tenth day after operation the tumor was found to have
increased in size by almost one-half, and the gain in size seemed
mostly toward the right and below. The new outlines of the enlarged
organ were marked on the patient's abdomen. Two days later a still
further very rapid increase in size was apparent, so that the anterior
surface of the mass presented an area twice as large as when the
patient entered the hospital. The incisions of the original explor-
ation were firmly healed by first intention. To-day for the first
time petechial hemorrhages were seen on the sides of the chest in
areas the size of the palm of the hand, and smaller similar purpuric
spots appeared on the right forearm and hand.

No change in subjective symptoms accompanied these new phenomena. The patient was still apathetic and weak, though he declared he felt better, and his only complaint was the exhaustion attendant on frequent bowel movements which still were of a tarry color and averaged five to six daily. The blood condition was examined from day to day, and showed practically the same condition as given above.

The question of splenectomy in the case had been constantly before the surgeon's mind, but he desired first to improve the patient's general condition in view of the recent enormous loss of blood he had suffered. The rapid and sudden increase in the size of the spleen, however, convinced Dr. Allen that ground was being lost instead of gained, and an immediate operation was proposed and accepted by the patient and his friends.

*Operation October 29th* (Dr. Dudley P. Allen. Gas and ether). *Laparotomy; splenectomy; closure.* A vertical incision 15 cm. in length was made separating the fibres of the left rectus muscle in order to avoid the former incisions. On opening the peritoneum some clear fluid was met with from which cultures were taken. The spleen was found to be lying free in the abdomen without adhesions to the intestines or other structures, its only attachment being a large long pedicle containing four twists, composed of large congested vessels, some of which contained thrombi. A more detailed, microscopic description of the organ and its pedicle will be given later.

The pedicle was securely tied high up with silk, clamped off distally and removed with the organ, which was with difficulty squeezed through the skin incision. No hemorrhage accompanied the removal; the pedicle stump was reinforced by over-and-over catgut stitches, and showed the openings of several large vessels.

The abdomen was closed in layers. The patient seemed to receive no shock from the operation which lasted twenty minutes.

For two days after operation the patient's general condition was encouraging. The temperature approached the normal, and the pulse rate decreased to an average of 90, with improvement in its quality. Stimulation with strychnine and saline subcutaneous infusions was continued as before.

On the third day a marked œdema of the whole right leg appeared which increased rapidly to alarming proportions. This was followed some days later by œdema of the right side of the scrotum and left side of the neck. Vomiting reappeared on the sixth day, and it became difficult to nourish the patient, as rectal nutrition was not retained except at intervals. There was no further appearance of blood, however, either in the vomitus or stools. Purpuric areas remained unchanged. Later the vomiting ceased and the patient seemed much brighter again. An attempt was made to give Fowler's

solution, but this had to be abandoned, as on the eleventh day the patient again rejected all nourishment. The abdomen, which up to this time had been flat, now began to show distention, with appearance of free fluid in the flanks. This collected rapidly, and on the thirteenth day the abdominal wound, which had healed and from which the stitches had been removed, burst open and a large amount of clear fluid escaped, from which cultures were sterile.

The patient now was irritable and very hard to rouse, sleeping nearly all the time with some delirium. Nourishment was refused, and rejected when given. Stools and urination were involuntary. This condition of progressive weakness, accompanied by emaciation, dyspnœa, and cyanosis, continued until the patient's death on November 15th, seventeen days after operation.

The changes in the blood following the removal of the spleen were very interesting, and in the main coincided with observations reported under like conditions in other cases, though, unfortunately, the patient's death prevented their being followed out over a long period.

Immediately after operation there was a great diminution in the red corpuscles from 3,480,000, four days before operation, to 1,836,000 two days after operation. This could not be accounted for by hemorrhage, either before or during the operation, as there was no great loss of blood immediately before the operation and no blood was lost in tying off the pedicle of the spleen. It must be attributed to the effect of the removal of the organ. After this initial drop the red count began steadily rising and had reached 2,800,000 just before death.

The white count which had been 8500, jumped to 34,000 two days after operation and gradually decreased to 22,000 at death. The percentage of hæmoglobin which before operation was 25 per cent., dropped to 22 per cent. after operation, and then gradually rose to 28 per cent. All these changes, the marked postoperative diminution in red cells, and to a less degree in hæmoglobin, and the sudden rise in leukocytes, corroborate previous experiences following splenectomy.

In the differential counts the polymorphonuclear form showed a marked increase from 74 per cent. before operation to 93 per cent. before death. The eosinophiles varied in amount. Nucleated red forms which averaged 6 in a count of 600 cells before operation increased to 36 before death.

To facilitate comparison the results of the various counts are tabulated :

|  | Date. | Red cells. | Leukocytes. | Hæmoglobin. |
|---|---|---|---|---|
| Before operation . . . | October 16 | 2,800,000 | 8,000 | 25 per cent. |
|  | " 25 | 8,480,000 | 8,500 | 25 " |
| After splenectomy . . . | November 2 | 1,886,000 | 84,800 | 22 " |
|  | " 8 | 1,914,000 | 80,000 | 28 " |
|  | " 7 | 2,212,000 | 22,000 | 22 " |
|  | " 10 | 2,848,000 | 28,720 | 28 " |
|  | " 11 | 2,464,000 | 26,000 | 26 " |
|  | " 12 | 2,568,000 | 28,000 | 27 " |
|  | " 18 | 2,632,000 | 22,000 | 28 " |
|  | " 14 | 2,682,000 | 22,000 | 28 " |

DIFFERENTIAL COUNTS OF 600 CELLS.

|  | Date. | Polymorpho-nuclear. | Small mononu-clear. | Large mononu-clear. | Trans-itional. | Eosino-philes. |
|---|---|---|---|---|---|---|
| Before operation | Oct. 25 | 74.0 per ct. | 18.0 per ct. | 4.0 per ct. | 1.5 per ct. | 2.5 per ct. |
| After splenectomy | Nov. 2 | 88.5 " | 12.75 " | 1.75 " | 1.50 " | 0.5 " |
|  | " 7 | 89.0 " | 4.66 " | 2.88 " | 2.0 " | 2.0 " |
|  | " 10 | 98.0 " | 8 8 " | 1.4 " | 0.6 " | 1.2 " |
|  | " 18 | 92.8 " | 8 6 " | 1.8 " | 1.0 " | 1.8 " |

2. PATHOLOGY. (Dr. Dolley.) *Autopsy Protocol.* (Autopsy performed seventeen hours after death.) The body is that of a well-formed but emaciated white man, 180 cm. long. There is moderate rigor mortis, and slight posterior hypostasis. The conjunctivæ are somewhat yellow. The mucous membranes are pale. The skin is sallow but not pigmented. A few small petechial areas are scattered just above the costal border. There is no glandular enlargement.

The chest is barrel-shaped. The supraclavicular fossæ and sternal notch are deep. The abdomen is scaphoid. Two recently healed wounds of operation appear in the midline; one, 6 cm. long, beginning at the xiphoid cartilage, the other, 7 cm. long, beginning at the umbilicus. A third laparotomy wound, healed with the exception of one stitch, 12 cm. long and 3 cm. to the left of the umbilicus, is present in mid-abdomen. The right leg is larger than the left throughout, and moderately œdematous.

*Brain* and *spinal cord* not examined.

*Abdominal Cavity.* The spleen is absent. The splenic veins become very tortuous from the end of the pancreas, one and one-half coils being left after the splenectomy. They measure from the end of the pancreas to their ligated extremity 2.5 cm. coiled and 5 cm.

uncoiled. The apposing surfaces of the coils are united by well-organized adhesions. Beginning at the junction with the portal vein, the splenic vein and its branches become more and more distended with palpably soft material until at their ligated extremity the larger of the two branches is 2 cm. in diameter. The veins are attached to the jejunum at one spot, 2 cm. in diameter, by organizing fibrinous exudate. On incision they contain soft mixed thrombi, which in places are loosely attached to the wall. There is slight thickening of the walls but no evidence of calcification.

The *splenic artery* is rather tortuous and dilated. It measures 2.5 cm. from the end of the pancreas to its ligated extremity. Its elasticity is poor, the intima is somewhat roughened and extremely reddened toward the distal end. It contains a similar grayish-red thrombus.

*Mediastinal fat* is scanty. The *thymus* is absent.

*Pleural Cavities.* Each contains about 10 c.c. of clear serous fluid. There are no adhesions.

The *pericardial cavities* contain 30 c.c. of similar fluid. The sac wall is not thickened.

*Thyroid Gland.* Both lobes are somewhat enlarged. The tissue appears normal.

The *tracheal glands* are markedly anthracosed. One at the bifurcation is studded with small fibrocaseous tubercles.

The *lungs* are voluminous, externally smooth and slightly anthracosed. They are hypercrepitant and cushiony except in the lower posterior portions. On section there is moderate hypostasis of the lower lobes. Elsewhere the tissue is more moist than normal. The left weighs 550 grams, the right 549 grams.

The *bronchi* contain some frothy watery mucus.

The *bronchial glands* are like the tracheal. One is composed of a calcified envelope with a caseous centre.

The *heart* is of normal size. The right ventricle averages 4 mm., the left 15 mm. in thickness. The auricles and right ventricle contain post-mortem jelly clots. Fluid blood is scant. The muscle is pale and flabby. The valves are normal except for a few atheromatous patches on the ventricular surface of the right mitral segment. The circumferences of the valvular orifices are: aortic, 6.2 cm.; pulmonic, 7.3 cm.; mitral, 9.5 cm., and tricuspid, 13 cm. The coronary arteries have a roughened intima with considerable atheroma. They are not tortuous. The endocardium elsewhere is smooth.

*Aorta.* The elasticity is normal. The wall is not thickened. The intima in places is roughened by yellowish or whitish plaques.

The *pulmonary artery* and *venæ cavæ* appear normal.

The *liver* weighs 1356 grams. It measures 27 x 14 x 8½ cm. The left lobe measures 13½ x 14 x 5 cm. It is contracted, but its shape is fairly preserved. The capsule is slightly thickened, and the

capsular veins are moderately injected. The veins of the round ligament are not dilated. The surface is moderately roughened and nodular, especially over the inferior and lateral portions of the right lobe. Over the inferior surface are several nodules softer in consistence than the rest of the tissue. On section, the organ is moderately hyperæmic. The cut surface is uneven and finely, though not uniformly, granular. The tissue is firm and cuts with increased resistance, especially in the lower and lateral portions of the right lobe, just under the capsule. The lobular outlines are not distinct; the tissue is markedly bile-stained, of a dirty brownish-yellow color. Owing to the bile staining the character of the apparently increased connective tissue is not evident. Glisson's capsule is most affected.

The *portal vein* is not thickened and its intima is smooth; it is free from thrombi.

The *gall-bladder* is constricted at the junction of its proximal and middle thirds and bent upon itself, so that the two portions are in partial apposition and united by old adhesions. Elsewhere it is non-adherent and apparently normal, containing dark bile. The ducts are patent.

*Œsophagus.* Congested sub-mucosal veins are distinct about the cardiac orifice.

The *œsophageal veins* are considerably dilated and tortuous. The coronary veins of the stomach are not so dilated, but the cardiac branches communicating with the œsophageal veins show marked varicosity.

The *stomach* is somewhat dilated, but the wall is not appreciably thinned. It contains 500 c.c. of brown sour-smelling fluid. The mucosa shows considerable post-mortem change and is not indurated. The sub-mucosal veins about the cardia and along the greater curvature are dilated. The folds of the mucosa only appear along the greater curvature, where their prominence is due to dilated veins. No eroded veins are apparent. There are no ulcers nor scars.

The *pancreas* is moderately hyperæmic. The head and body are of normal size, but are distinctly indurated. The tail is very contracted and firmly attached to the splenic vessels. On section there is great increase of dense fibrous tissue.

The *small intestine* is not distended. It shows only an occasional congested but not swollen area in the mucosa. The veins of the serosa are not congested.

The *appendix* is normal.

*Large Intestine.* The mucosa of the cæcum and the ascending colon is markedly congested. There are no hemorrhoids.

The *suprarenals* show post-mortem softening of the medulla.

*Kidneys.* Right weighs 215 grams, the left 285 grams. They measure respectively 12 x 7.5 x 3.8 and 13 x 8.6 x 7 cm. Perirenal

fat is scanty. The cortical veins are not dilated. The capsule is normal.

The cortex of the right is 6 mm., of the left 8 mm. in thickness. The cut surface is smooth, but mottled with grayish areas corresponding to the labyrinths. The organs are moderately pale and the glomeruli are barely visible. The arteries are not sclerotic.

The *ureters, bladder, seminal vesicles, prostate,* and *testicles* appear normal.

The *mesenteric glands* are small and barely palpable.

The *retroperitoneal glands* are enlarged, firm, and of a glistening grayish-white appearance on section.

*Hæmolymph Glands.* Lying on both sides of the sternum, along the carotid arteries, the renal vessels, the iliac vessels, and about the splenic vein and the œsophagus appear glands varying in size from a pinhead up to that of a large bean. These are soft, dark-red, spleen-like and fairly abundant. Between thirty and forty of convenient size were removed.

The *right iliac vein* just above Poupart's ligament is filled with a red, non-adherent thrombus.

The *right femoral vein* contains a similar thrombus. This changes in character 5 cm. below Poupart's ligament, having a white friable core which at one point is attached to the wall.

The *inferior hemorrhoidal veins* are moderately dilated and tortuous.

*Bones.* Several ribs and the right femur were opened and found to contain bright-red and succulent marrow. No lymphoid areas appear.

*Spleen* (received from the surgical department. Gross description by Dr. Howard). The specimen consists of a spleen, irregularly oval in shape, presenting a rounded anterior margin from which the notch has been obliterated. It weighs 1650 grams and measures 22 x 16 x 7 cm. The vessels, which form a pedicle, are covered with fine pinpoint fibrin masses, but present no adhesions. This pedicle is twisted four times, and its uncoiled state measures 17 cm. in length and 4 cm. in its greatest diameter. It is composed of several large tortuous veins surrounded by a considerable amount of fat, and several branches of the splenic artery, which is divided a considerable distance from the hilus. The pedicle also includes a soft body measuring 1.5 x 1 cm., covered with peritoneum, and resembling an enlarged lymphatic gland. At the distal end mixed gray and red thrombi protrude from the veins. The largest vein is 2.5 cm. in its greatest diameter. On incision they are filled with thrombi, but contain a variable amount of thin fluid blood. The thrombi are partly red and partly mixed, some being yellowish-gray in color. As a rule they are non-adherent, or can be easily separated. In general the mixed thrombi are soft or friable. The thrombi can be readily traced into the large and the small veins of the organ.

The walls of the veins are not much thickened, and show no signs of recent or old inflammation except the thickening of one near the hilus.

The splenic tissue is light brown in color and œdematous. The trabeculæ are well marked, the lymph nodes obscure. The tissue is not friable. There are no infarcts.

*Microscopic.* Material from all organs was hardened in Zenker's and Orth's fluid, in formalin and in alcohol, and stained by ordinary and special methods.

*Lungs.* There is moderate emphysema and anthracosis. The sections from the posterior portions show moderate congestive œdema. The bronchi and pulmonary arteries are normal. Careful search for the bone-marrow giant cells described by Warthin in his cases was negative.

*Heart.* There is marked segmentation and some fragmentation of the muscle.

*Liver.* The connective tissue is moderately increased, but not at all uniformly even in the same section. The increase is greatest in the right lobe under the capsule, as noted macroscopically, Glisson's capsule about the larger vessels being particularly thickened. The lobules are usually sharply defined, but occasionally the connective tissue extends somewhat into them. The connective tissue is dense fibrous in character, with few nuclei, and slight round cell infiltration. In places of more marked fibrosis, fibroblastic cells are more abundant, but the tissue is nowhere actively proliferating. More rarely an increase of fibrous tissue about the central veins is noted. Mallory's connective-tissue stain shows here and there a slight increase of the reticulum of the lobules. This is more prominent in areas of atrophy of the lobular centres. This reticulum takes a light red with Van Gieson's stain. A very few fibroblastic cells appear in these areas and several capillaries are filled with proliferating endothelial cells with a few karyokinetic figures. Excepting these few instances endothelial proliferation does not occur. In the more cirrhotic portions many lobules show dilatation of the central veins and capillaries with some atrophy of the liver cells, but this is appreciable in but few lobules in the less fibrosed areas. The atrophic liver cells present more or less fatty degeneration and necrosis, with a little brownish-yellow pigment. Numerous attempts to demonstrate the presence of iron were unsuccessful. Proliferation of bile canaliculi is found in only two areas. No bone-marrow giant cells are found.

The *stomach* and *intestines* show chronic passive congestion, associated in the small intestine with slight chronic catarrhal inflammation.

*Pancreas.* Sections from the head and body show a moderate increase of connective tissue, both perilobular and interacinous. Some islands of Langerhans also have an increased amount of

stroma. The sections from the tail show marked fibrosis, dense fibrous and hyaline tissue replacing many lobules, while the remaining ones are small and distorted. The ducts have a thickened wall and a few are tortuous. The islands of Langerhans are diminished in number. A few are unaffected. In some there is fibrosis, but in others fatty and granular degeneration of the cells is more pronounced. The veins are moderately congested and have thickened walls, particularly in the tail.

The *kidneys* show a very slight chronic interstitial nephritis. There is no deposition of pigment.

The *portal* vein is normal.

*Splenic Veins.* The intima is slightly and irregularly thickened and is composed of dense fibrous tissue with few nuclei. Thickening of the adventitia is more pronounced. In the latter, particularly about the vasa vasorum, there is moderate fibroblastic proliferation. But few fibroblastic cells occur in the intima and media. Organization of the thrombi is well advanced in places.

The *mesenteric glands* are fibrosed. There is some proliferation of the endothelium.

*Hæmolymph Glands.* A few are of the marrow lymph type described by Warthin, but show partial transformation into ordinary lymph glands. The lymph spaces are full of endothelial cells, some of which are phagocytic for red blood and lymphoid cells. Only a moderate number of bone-marrow giant cells appear.

The majority of the hæmolymph glands resemble splenic tissue in structure. The follicles contain no germinal centres and usually show small hyaline areas. The blood sinuses, which are much dilated, are only partly filled with blood. The most striking feature is the presence within them of numerous large cells of endothelial type packed with red blood cells. Mononuclear eosinophiles appear in great numbers, and normoblasts are moderately numerous. A few mastzellen are present. Numerous cells resembling myelocytes appear in the blood sinuses, but these are more abundant in the lymph spaces of the glands of marrow lymph type (Wright stain). Pigment is in moderate amount. It gives the iron reaction with ferrocyanide and HCl. Some phagocytic cells give the same reaction in a diffuse way.

The *bone-marrow* (rib) is of a poor lymphoid type. Giant cells are not apparently reduced in number. Plasma cells and polymorphonuclear leukocytes are in small proportion, but mononuclear eosinophiles with nuclei varying greatly in size are extremely abundant. Polymorphonuclear eosinophiles, while absolutely increased, are less numerous relatively. Normoblasts appear in large numbers with active mitosis. Myeloblasts are only occasionally seen. Neutrophilic myelocytes are almost entirely absent. A peculiar feature with the Wright stain is the presence of cells

resembling lymphocytes, but with a red protoplasmic border.   Excluding these, ordinary lymphoid cells are not increased in number.

There is a scanty amount of iron containing pigment, both in cells and free.

*Spleen.*   The capsule is moderately thickened and composed of a dense hyaline connective tissue.   The trabeculæ are also thickened and are farther apart than normal.   The splenic tissue is constructed of considerably dilated blood spaces, more or less filled with blood, and separated by a moderate amount of usually dense fibrous tissue with a varying number of fibroblasts.   Under the capsule this newly formed connective tissue is much more abundant, and it is not uniform in the other sections, thick fibrous bands appearing here and there.   Hyaline transformation of the connective tissue appears nowhere outside of the trabeculæ proper. The venous spaces are lined either by an almost flat or a somewhat swollen endothelium with an occasional free cell, but no proliferating endothelium appears.   Scattered through the pulp are relatively few lymphoid cells and an almost equal number of polymorphonuclear leukocytes.   The lymph nodes are farther apart than normal, but it is not possible to say they are absolutely diminished in number.   They are usually not atrophic but show an increase of coarse reticulum with a few fibroblasts.   Often the central arteriole is thickened and hyaline.   The veins are greatly dilated, their walls are moderately thickened and many contain fibrinous and mixed thrombi.   Not infrequently small fibrinous clumps appear in the blood spaces.

A very moderate amount of pigment is deposited in phagocytic cells in the blood spaces or in the stroma or lies free in the trabeculæ. It gives the iron reaction.   A few normoblasts, plasma cells, and mononuclear eosinophiles are to be seen, but neither myelocytes nor bone-marrow giant cells are found.

With the Van Gieson stain there is considerable variation, but a large part of the newly formed stroma takes a deep-red color.   A section throught one of the splenic veins removed at operation shows the same degree of fibrous thickening as in the stump.   The adventitia is the seat of a much more marked fibroblastic proliferation.   The thrombus is just beginning to organize.

*Pathological Summary.*   There is nothing in the histological structure of the spleen which cannot be explained simply by chronic passive congestion.   In the causation of this, two factors have to be considered—*i. e.*, the abnormality of the splenic vessels and the cirrhosis of the liver.   The dislocation of the spleen must have been of long standing, for the splenic vessels uncoiled measured 19.5 cm. from the end of the pancreas.   Granting even that the multiple twists all occurred as a result of the accidents, which is hardly probable, the elongation which existed prior to this must have caused considerable interference with the splenic circulation.

In two cases of splenic anæmia, reported by Dock and Warthin, there were stenosis and calcification of the portal vein, a condition identical with this one as far as the effect on the spleen is concerned. The question they raise is whether the portal lesion is primary and the splenic fibrosis secondary to it, or, on the other hand, whether the splenic condition is primary, while the condition of the portal vein is coincidental or results from a toxic condition of the portal blood dependent upon the disturbed splenic function or dependent upon a portal or general intoxication. The dislocation of the spleen could not have been of congenital origin, for the alteration does not indicate such a long-standing condition, and an enlargement of the organ at once suggests itself as the main factor in its production.

The abnormality of the splenic vessels is essentially a mechanical, not an organic one. Granted that some enlargement of the spleen, from whatever cause, started the elongation of the splenic vessels, once produced, with probably some torsion, the reaction on the circulation of the dislocated organ would be so great that the subsequently increased congestion and fibrosis would result largely from the condition of the vessels. The condition of the spleen must be considered then as largely secondary to that of the vessels, which gives them a very probable etiological significance. If splenic anæmia existed before the dislocation of the spleen, and the initial enlargement and the dislocation of that organ were manifestations of the pathological processes of the disease, the splenic vessels lose their casual relationship. But the histological structure offers no evidence of this. There is not even the proliferation of endothelium so commonly found in the spleen in this disease to complicate the picture.

The relationship of the cirrhosis of the liver to the condition in the spleen presents the greatest difficulty in interpretation. In part the process in the liver is regarded as a mild and not uniform chronic passive congestion, with a just beginning central cirrhosis, shown by the increase of fine reticulum in the atrophic portions of the lobules, with some endothelial proliferation. The moderate emphysema of the lungs offers a probable explanation for this condition. More important there is also a moderate though irregular increase of periportal tissue, but the histological pictures of the fibrosis in the liver and in the spleen are too nearly identical to draw conclusions regarding time relationship. What part the liver played in the production of the splenic condition it is impossible to say. Was the hepatic process primary, and was the initial enlargement of the spleen leading to its dislocation secondary to it, or were the two processes coincident? The fibrosis in the liver and in part that in the spleen may have resulted from a general or portal intoxication.

The changes in the hæmolymph nodes are interpreted as compensatory for the failing splenic function. It is probable that the bone-

marrow shared to some degree in the assumption of this function. But the presence of pigment and phagocytes in the spleen would, however, indicate that this function was not entirely lost, while the moderate evidence of old hæmolysis in the hæmal glands would further bear this out. But these glands show an excessive number of phagocytes full of intact red blood cells which is readily explained by the results of Warthin's work. He concludes from his experiments with sheep that hæmolysis and leukocyte formation are the functions taken up by the hæmal glands after splenectomy. But the hæmolytic action of these glands exceeds that of the normal spleen, and the resulting anæmia is compensated for by increased activity on the part of the bone-marrow. The marked fall in the blood count after splenectomy was due then to this excess of hæmolymphatic hæmolysis over that of splenic.

No iron pigment could be demonstrated in the liver and kidneys. This fact, together with the paucity of megaloblasts in the bone-marrow, indicates that the anæmia was not primary in type. While the hyperactivity of the hæmolymph glands would explain the anæmia which undoubtedly existed before the accidents, the intestinal hemorrhages following them reduced the patient to his state on entering the hospital.

*Pathological Diagnosis.* Dislocation of the spleen with marked elongation and torsion of its vessels, and thrombosis. Chronic passive congestion and fibrosis of the spleen. Interlobular atrophic cirrhosis of the liver. Chronic passive congestion with beginning central cirrhosis of the liver. Chronic passive congestion of rest of portal system. Compensatory hyperplasia of hæmolymph nodes. Hyperplasia of the bone-marrow. Secondary anæmia. Moderate diffuse emphysema of the lungs. Tuberculosis of bronchial and tracheal glands.

My thanks are due to Dr. W. T. Howard, Jr., for the use of material and for his interest in the work.

3. GENERAL SUMMARY. The patient's previous history of pallor, digestive disturbances, and pain in the splenic region, symptoms of which there is a history for a number of years, strongly suggest the early stage of a splenic anæmia. The frequent urination and the pain in the splenic region also would imply a long-standing dislocation of the spleen. This is corroborated by the enormous elongation of the splenic vessels. Whether or not all the twists in the splenic veins occurred at the time of the two accidents, it is impossible to state, but it is at least more reasonable to suppose that from their multiple character they did not all occur at one time, but that some had existed previously.

The thrombosis of the splenic vessels must have been the cause of the sudden enlargement of the spleen while the patient was in the hospital. The lack of organization in the thrombi of the vessels removed at the splenectomy proves this.

If Banti's stage of splenic anæmia is limited only to those cases
in which the cirrhosis is a terminal manifestation we cannot include
our case in that category, for the cirrhosis of the liver is certainly
of as long standing as the fibrosis in the spleen.   We prefer to
regard the case as one of splenic anæmia associated with a cirrhosis
of the liver, not as a result of the process in the spleen, but rather
accompanying it.

The enormous elongation and torsion of the vessels associated
with the dislocation of the spleen possess a very probable etiological
significance in this case.

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## PUS IN ABDOMINAL OPERATIONS.[1]

BY

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THE mortality following operations for suppurative disease of the tubes and ovaries is variously estimated as from 8 to 20 per cent. In the face of these figures it is certainly incumbent upon us not to rest satisfied with present conditions, but ever to be looking for more perfect methods and to adopt more stringent precautions in our operative procedures. The most perfect degree of asepsis obtainable before, during, and after these operations, must always be insisted upon. Whenever pus is met with at the time of the operation, if a fatal result occurs, we are too apt to content ourselves with the explanation that infective material was already present and that its spread was only a natural result. As a matter of fact, however, it must not be forgotten that the pus met with under such circumstances, as a rule, is free from virulent bacteria; and whenever an infection follows a "pus operation" and no organisms can be demonstrated in the secretions encountered, it is not only possible, but even highly probable, that in the majority of these instances the fatal results have been due to the introduction of some septic material during the operation.

Again, as a result of my observations during the past seven years, I have become convinced that operators not infrequently err in carrying out radical abdominal procedures, when the patient's resistance is in such a lowered condition that she is very apt to succumb to the shock of the operation *per se.* Such a condition must always be given careful consideration when deciding for or against operative interference during an acute attack of localized or more or less generalized pelvic peritonitis. Believing that this factor has a very important significance in influencing our results, I have made it a rule, during the acute stage of a pelvic abscess, to defer an operation while the patient's condi-

[1] Read before the American Gynecological Society at Chicago, May 31, 1901.

tion is improving. In the meanwhile the patient is kept perfectly quiet on her back in bed, and heat, in the form of flaxseed poultices or turpentine stupes, is applied to the abdomen. In addition, a vaginal douche of a gallon of a warm one per cent solution of carbolic acid or a saturated boric acid solution is given twice daily. For nourishing the patient we depend upon nutritive injections entirely for several hours. Anodynes and heart stimulants are given if necessary. As a result of these measures we have found that, in the great majority of cases, the acute symptoms will subside within a few days and we can then operate upon the patient, who is now in a much better condition, either by the abdominal or the vaginal route or by the combined procedures. If, however, no improvement takes place under the above treatment within a reasonable time (eight to ten hours), and if we can make out a pelvic mass, we puncture through the vagina, and, after irrigating the sac or the pelvic cavity, pack with sterilized gauze. We have noticed that a number of well-known general surgeons in this country are treating cases of acute appendicitis in a similar manner.

The micro-organisms that are most frequently met with in cases of suppurative disease of the tubes and ovaries are Staphylococcus pyogenes aureus, Streptococcus pyogenes, Gonococcus, and Bacillus coli. Other forms are occasionally met with, such as the tubercle bacillus and Proteus Zenkeri.[1] When we are able to demonstrate the presence of Staphylococcus pyogenes aureus at the time of the operation, we expect an uninterrupted convalescence in the majority of these instances. The organism most to be feared is Streptococcus pyogenes, and its presence always makes the prognosis very grave. We recall in particular an instance in which at the time of the operation macroscopical evidences of a small amount of pus were demonstrable, but no organisms could be shown from the pus at the examination made at this time. The culture tubes that were inoculated at the time of the operation, however, subsequently showed a profuse streptococcus growth. We drained in this case, but, despite our efforts, a streptococcus peritonitis developed and the patient died. The same organism was found at the autopsy. We unfortunately infected another patient with this organism, although before the second operation we carefully sterilized our hands, instruments, etc., in the usual manner. We removed without much difficulty the adherent tubes and ovaries on both sides. Cover-slips made at the time of the op-

[1]Johns Hopkins Hospital Bulletin, No. 70, January, 1897.

eration were negative. In two days, however, this patient began to show evidences of a peritonitis, and a fatal result took place a day and a half after the death of the first patient. Streptococcus pyogenes was found, at the time of the autopsy, in the exudate present in the peritoneal cavity. In the first case there was a history of an induced abortion at the third month of pregnancy with subsequent fever six years before admission to the hospital. This suggested a streptococcus infection at that time. In the second case the patient had had two normal labors without any complications.

Such a stern lesson taught us once for all that even in cases in which there are only adherent organs, even when no pus is apparently present, we should always be on our guard against carrying infective material from one case to another. From the fact that we found no organisms present by the cover-slip examination at the time of the operation, however, we felt that we were justified in going on with the second operation. But for several years now, after having had such an experience, we do not perform more than one abdominal section in the same day, preferring to operate much more frequently rather than run risks. I certainly believe that the adoption of this precaution has saved a certain number of cases from being infected. I should say that, even prior to this regrettable accident, whenever we encountered a pus case we always postponed the carrying out of any further abdominal work, except in emergencies, until forty-eight hours had elapsed.

The question of using drainage in pus cases is always of interest, and all operators are not in agreement as to its advantages and disadvantages. In my clinic we have not used a drainage tube during the past seven years, and we now, as a matter of fact, seldom drain, even in pus cases, through the abdominal incision. Occasionally, when there has been a septic area left behind, we drain *per vaginam*, but even in these cases I do not feel that this procedure is by any means always necessary.

It has always seemed to me that we do not sufficiently protect from infection during the operation the portions of the pelvic contents which are apparently intact. Inasmuch as pelvic inflammatory disease frequently involves the intestines to a wide extent, it is sometimes impossible to prevent the infectious material from being spread more or less during the manipulations of the diseased structures. We can, however, to a great degree limit the free distribution of this purulent material throughout the abdominal cavity. In order to effect this, as soon as the ab-

domen is opened we are in the habit of placing large gauze sponges high up in the flanks on either side, the patient being kept in the horizontal position while the masses are being enucleated. If we break into a pus sac during our manipulations, we at once make cover-slips of the escaped pus, and while these are being examined we attempt, as far as possible, to remove the material that has escaped by mopping it up with gauze sponges. After this we wash out the abdominal cavity with large quantities of sterile salt solution, in order to get rid of as much as possible of the pus and to dilute any that may remain. The enucleated mass is now surrounded with gauze moistened in a 1:1000 bichloride solution, which is not removed until the structures have been cut away. The pedicle is thoroughly cauterized with the Paquelin cautery, and the abdomen is again washed out with salt solution, sponged dry, after which 300 to 500 cubic centimetres of warm sterilized salt solution are introduced and left there. The incision is closed without drainage.

The following is the clinical and bacteriological analysis of 72 consecutive, unselected abdominal sections for suppurative diseases of the tubes and ovaries, two deaths occurring:

ANALYTICAL REPORT OF SEVENTY-TWO CONSECUTIVE PUS CASES.[1]

*Age.*—The oldest patient was 41, the youngest 17, the average age being 26.37.

Fifty were married, 16 were single, 6 were widowed.

*Occupation.*—Housework, 43; prostitutes, 11; dressmaking, 3; cooks, 2; canvassing agents, 2; seamstresses, 2; boxmaker, 1; dining-room girl, 1; clerk, 1; domestic, 1; laundress, 1; cigar packer, 1; match factory girl, 1; pianist, 1; telephone clerk, 1.

In 23 pregnancy had not occurred. In 13 miscarriages alone had taken place. In 8 full-term births alone had occurred. In 28 there was a history of births at term and miscarriages. The highest number of miscarriages in any one case was 5. The highest number of births at term in any one case was 7. The average number of miscarriages in the 41 cases having miscarriages was 1.94 per cent. The average number of births at full term in the 36 cases having births at term was 2. Thus it will be seen that in 49 of the 72 cases the number of births at term was 2. These figures go to show that the accidents inci-

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[1] The first case of this series was operated upon October 11, 1898, and the last one February 28, 1901. Since the analysis of these cases we have had 15 additional instances, making the number 87, but a sufficient interval of time has not elapsed from which to draw conclusions.

dental to labor and abortion have to be carefully considered as factors in the production of pelvic disease.

*Infection.*—We were able to establish a gonorrheal history in 14 cases (probable in 4 others). Infection after labor at term had occurred in 7 cases (2 of these cases also gave a history of a previous gonorrhea); infection after miscarriage in 17 cases (4 of these patients giving also an old gonorrheal history). In the remaining cases (31) no definite history of a specific infection or any relation between the disease and labor or abortion could be made out. In many cases there was a gradual onset with exacerbations of the symptoms at the menstrual period, but with no definite acute attack before admission into the hospital. In many the symptoms had persisted for long periods of time, in 1 case for 20 years. It was frequently noted that an attack of peritonitis had occurred before the patient was admitted into the hospital. In 33 cases these attacks had lasted under three weeks, and for the most part they were of about two weeks' duration. The shortest attack was one of two days immediately preceding admission. In cases of more than three weeks' duration various periods of time were represented—six weeks, two months, six months, a year, etc., with no special uniformity. Definite and similar previous attacks had occurred in 7 gonorrheal cases, the largest number of previous attacks being 3, except in 1 case in which there was a history of a great many. From this it will be seen that the infections following gonorrhea on the one hand, and labor or abortion on the other, are about equal in number. Thus, in 14 cases (19.44 per cent) we were able to get a positive history of a previous gonorrheal infection, and in 20 cases (27.77 per cent) there had undoubtedly been an infection following labor or miscarriage. Allowing, however, for those cases in which there had been a previous gonorrhea as well as a history of an infection following labor or abortion, and placing these doubtful cases in the column of the gonorrheal infections, we have the following figures: Gonorrheal cases 23 (?), or 33½ per cent of the cases; infections after labor and miscarriage, 20, or 27.77 per cent of the cases. Here, as has been said, we have added to the gonorrheal list by taking six cases which would seem to rather come under infections following labor or miscarriage. It is, of course, often extremely difficult to feel sure that a patient has had a specific vaginitis, unless cover-slip examinations have been made of the secretions at the time of the supposed infection. In many instances it is

not difficult to obtain a history of a vaginitis, but to prove that it has been specific in origin is not always easy. Many of the miscarriages had been criminally produced. The infections in these cases could generally be traced to the production of the abortion.

The temperature, pulse, and respiration before operation were as follows:

Highest temperature, 105.2° F.; pulse, 142; respiration, 42. Lowest maximum temperature, 98.18° F.; pulse, 82; respiration, 22.18. Average maximum temperature, 102.09° F.; pulse 106.8; respiration, 27.2.

The chief clinical symptoms were as follows, many patients showing several:

| | | | | |
|---|---|---|---|---|
| Pain in lower part of the abdomen was present in 67 cases. | | | | |
| Backache ...................... | " | " | " 43 | " |
| Leucorrhea .................... | " | " | " 34 | " |
| Dysmenorrhea .................. | " | " | " 30 | " |
| Headache ...................... | " | " | " 21 | " |
| Dysuria ....................... | " | " | " 13 | " |
| Bearing-down pains ............ | were | " | " 8 | " |
| Menorrhagia ................... | was | " | " 5 | " |
| Constipation .................. | " | " | " 6 | " |
| Gastralgia .................... | " | " | " 2 | " |
| Chilly feelings ............... | were | " | " 2 | " |
| Metrorrhagia .................. | was | " | " 3 | " |
| Cough ......................... | " | " | " 1 case. | |
| Painful defecation............. | " | " | " 1 | " |
| Nausea and vomiting........... | were | " | " 2 cases. | |

The most prominent symptoms were pain in the lower abdomen, backache, a leucorrheal discharge, dysmenorrhea, headache, and painful micturition.

Pus was found as follows: In the ovary, unilaterally, 24 times; bilaterally, 5 times, including tuberculous cases. In the tube, unilaterally, 25 times; bilaterally, 39 times, with tuberculous cases. In the appendix, in 1 case. In the walls of the uterus, in 1 case. In almost every case in which the pus was unilateral, the other tube and ovary were found to be adherent. Infection of the tube and ovary together (tubo-ovarian abscess) was noted unilaterally only and in 17 cases. The tubes are more liable to a bilateral infection; the ovaries to a unilateral infection.

The following operations were performed, all being carried out at the Lakeside Hospital:

Appendicectomy ............................................. 26
Dilatation and curetting...................................... 24
Evacuation and drainage of pus sac, when removal was impossible  2

Whenever the tube or ovary was simply adherent, but not disorganized, the adhesions were separated and the structures allowed to remain. Despite this conservative surgery, in not a single case up to the present time have there been complaints from these patients, nor has there been any necessity for further operative procedures. As a supplementary procedure appendicectomy was carried out 26 times, or in 36.1 per cent of the total number of cases. We believe that, in cases of suppurative disease of the tubes and ovaries, in about one-third the appendix will be found to be adherent. In those cases in which vaginal puncture was carried out, we found it impossible to thoroughly remove the abscess wall by the abdominal route, and in such instances we employed drainage *per vaginam* for a few days. In 3 cases, after opening the abdomen, it was found impossible to remove the pus sacs owing to the patients' weakened condition, and we were therefore obliged to drain through the vagina.

*Results.*—2 patients died, 70 recovered. *Mortality* for all cases, 2.77 per cent. *Morbidity:* So far as we have been able to ascertain, there are no patients in this series that make any complaints referable to disorders in the pelvis.

*Drainage.*—In 9 cases drainage was carried out through the cul-de-sac alone; in 2 cases through the abdominal wall alone; in 1 case through the cul-de-sac and abdominal wall combined. In 2 cases in which infection occurred subsequently to the original operation, the abdomen was opened and drained. One of these patients died, the other recovered. Thus abdominal drainage was carried out in 2 instances only immediately following the operation, or in 2.77 per cent of the cases. In 10 cases (13.6 per cent) drainage was carried out *per vaginam*.

²In these cases the opposite tube and ovary were removed in all but one case, in which this procedure was impossible, drainage being used after evacuation of the pus.

Suppuration of the abdominal wound occurred in 12 cases, or 18.7 per cent. In 2 of these abdominal drainage was employed at the time of the operation. In 2 abdominal drainage was instituted several days after operation, 1 of these patients recovering. In the remaining 8 cases primary union occurred on the surface, but pus developed deeper down, usually about ten to fourteen days after the operation. Wherever there occurred a secretion from the wound in which it was possible to demonstrate micro-organisms, we classified the case as one of infection. In the secretion from the incision in 6 of the 12 cases we were able to demonstrate Staphylococcus pyogenes aureus and in the other cases Staphylococcus pyogenes albus. In this series of cases we consider that the infections above referred to were to some extent due to the fact that we had previously operated upon a case of post-puerperal infection in which Staphylococcus pyogenes aureus was found at the time of the operation. In six of the abdominal sections performed during the two weeks following (although we left an interval of four days) the incision became infected to a slight extent, and in the sero-sanguinolent secretion we were able to demonstrate Staphylococcus pyogenes aureus. In the tubes and ovaries the following organisms were found: Staphylococcus pyogenes aureus, 2 cases; Staphylococcus pyogenes albus, 1 case; Bacillus coli communis, 1 case; Streptococcus pyogenes, 2 cases; Friedländer's bacillus, 2 cases; Bacillus tuberculosis, 1 case; Gonococcus, 7 times positive (3 others probable). Thus in 12 cases (16 per cent) organisms were found. We were not able to cultivate the gonococcus, and the diagnosis was made entirely from the cover-slip examinations from sections of the tissues.

The diagnoses at the time of the operations were as follows (these differ somewhat from the pathological diagnoses, since a considerable number of cases of apparent salpingo-oöphoritis proved on further examination to be pus tubes):

| | | | |
|---|---|---|---|
| Abortion, retained secundines. | 1 | Endometritis, Septic | 1 |
| Appendix, abscess of | 1 | "        and stenosis | 1 |
| "    adherent | 11 | Follicular hypertrophy of ovary | 6 |
| "    concretions in | 2 | Hydrosalpinx | 1 |
| "    cystic | 1 | Lacerated cervix | 1 |
| "    flexure of | 2 | Myoma | 3 |
| "    (periappendicitis) | 6 | Ovarian abscess, unilateral[1] | 1 |
| Endometritis | 24 | "        "    bilateral | 1 |

[1]Seventeen cases of tubo-ovarian abscesses have been classified under pyosalpinx and ovarian abscess; in each instance the abscess was unilateral, with a pyosalpinx upon the other side in 12 cases.

Perhaps a few words about the two fatal cases may be of interest. In the first case, in which there was a uterus septus partialis, a hystero-salpingo-oöphorectomy for a tubo-ovarian abscess involving the uterine cornu, with appendicectomy, was performed. A considerable amount of pus escaped into the pelvis at the time of the operation, although the adjacent structures were protected by gauze pads. The previous history suggested the possibility of a streptococcus infection, since her illness had followed a miscarriage which had occurred ten weeks before the patient was admitted to the hospital. The temperature at the time of her entrance ranged between 100° and 102° F., but for the most part was under 102° F. At the time of the operation we were not able to demonstrate any organisms by cover-slip examination in the pus that escaped. We accordingly followed our usual plan of washing out the abdomen and closing without drainage. In eight hours the patient's temperature rose to 104° F. and the pulse to 148. She was, however, feeling comfortable. The next day her temperature fell to 101.5° and her pulse to 128. For the succeeding twenty-four hours her symptoms were on the whole favorable, and, with the exception of some difficulty in respiration, she seemed to be progressing satisfactorily. Her temperature varied during the next three days between 101° and 103.8° F.; at the same time there was marked dyspnea and the pulse gradually increased in rapidity. She finally died on the fourth day following the operation, without having shown any marked evidences of any peritoneal involvement, as there was no nausea, vomiting, or tympany and the bowels had been thoroughly well opened.

Autopsy showed the case to be one of pelvic abscess with general sepsis. Cultures made from the lung showed a pure streptococcus pyogenes infection, the same organism being also found in the liver, pleura, and peritoneum. In this case, then, we had to do with a streptococcus infection which had as its origin either

[1]This includes 3 tuberculous cases. There were 3 tuberculous cases of bilateral pyosalpinx; in 1 of these there was also a bilateral tuberculous abscess of the ovary.

[2]Many showed pus on microscopic examination.

the introduction of this organism at the time of the operation or the miscarriage which occurred some months previous to the time of the operation. From my previous experience I am of the opinion that in this case a fatal infection would have followed even if drainage had been used.

In the second case we were not able to establish a history of an infection following an abortion or labor. Here we had to deal with an abscess involving the left tube and ovary, and an adherent right tube. We removed the diseased structures and made a cover-slip examination of the pus, but no organisms were demonstrated. We also inoculated culture tubes. The abdomen was closed. The patient's temperature the day following the operation rose to 104.4° F., and for the next two days varied between 102.5° and 105.7° F. On the tubes that were inoculated from the pus streptococci were found. On the second day after the operation the abdomen was reopened under cocaine anesthesia and washed out, drainage being afterward instituted. The abdomen was irrigated a second time and salt infusions were carried out at stated intervals. She died on the third day.

Cultures made from the lung at autopsy showed the Diplococcus pneumoniæ and Bacillus coli communis; in the liver, Bacillus mucosus capsulatus was found, and in the peritoneum Diplococcus pneumoniæ. In this case, then, streptococci, though not demonstrable by cover-slip examination at the time of the operation, appeared in the culture tubes two days later. At the time of the autopsy only Diplococcus pneumoniæ was found in the peritoneal cavity.

In conclusion I wish to thank my former associate, Dr. William H. Weir, and my present associate, Dr. C. D. Williams, for kind assistance in making up this analytical report.

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# THE MORTALITY FOLLOWING OPERATIONS FOR PUS IN THE PELVIS.

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In the course of his everyday reading, as well as in his own operative work, the busy surgeon is always meeting with new data, so that at the end of a certain time he finds his mind loaded up with a mass of undigested knowledge, much of which is of no practical utility, or even apparently contradictory. Under these circumstances he finds it necessary to pass in review from time to time all these accumulated ideas, and to sift out the chaff from the wheat so that he can once more start with a clear field and find himself in a position to answer the questions: 1. What have I learned lately which I can utilize in improving my surgical judgment? 2. What omissions from or additions to my operative technic will give me better results in the future?. Probably the most satisfactory way by which he can attain this end is to make a careful classification of all his cases and as soon as he finds himself in possession of a sufficiently comprehensive series exemplifying a given pathologic condition to make a careful analysis of all the cases, and from the various data thus obtained to draw any conclusions that seem to be warranted, discarding what has proved to be worthless, and reserving for further consideration any points which may still be doubtful. It goes without saying that deductions based on a few isolated cases would be worse than useless and might be altogether misleading, and that the series should present instances of approximately all the various complications which may be met with in this particular class of operative cases.

During the past three years we have had in our clinic two series of unselected abdominal sections without a

death. In the first there were 114 and in the second
108 cases. In the two together we encountered prac-
tically all the usual forms of pelvic lesions that occur
in the female generative organs. From these cases, to-
gether with some prior and other subsequent instances, we
have been able to make up a series of 100 consecutive
abdominal operations for pus in the pelvis with two
deaths. An analytical report of 72 of these cases has
already appeared in a paper read before the American
Gynecological Society in Chicago, May 30, 1901. Since
the date of this publication we have had 28 additional
instances. To-day I will briefly consider some of the
bacteriologic questions connected with such pus cases,
together with some points in the operative technic.

So far as I can gather from my reading, many sur-
geons would appear to still hold to the belief that the
finding of pus in the Fallopian tubes and ovaries in a
given case affords sufficient ground for assuming that the
patient's chances of recovery following radical operative
procedures are necessarily bad. So gloomy a prognosis,
I feel sure, when based on the presence of pus *per se*,
is by no means always warranted, and the general con-
dition of the patient, as well as her capacity or inability
to react after the shock of a severe surgical operation,
are often of paramount importance. This is liable to be
the case more particularly when dense adhesions have to
be separated. Again, when pus is already present, not
a few operators appear to assume that the carrying out
of an aseptic technic, so far as they themselves are con-
cerned, becomes no longer necessary, and when a fatal
result follows an operation under these conditions or
when the abdominal wound subsequently becomes in-
fected, they are too apt to content themselves with the
explanation that infective material was already present
and its spread was only a natural result. Against such
conclusions, however, we have the evidence of repeated
bacteriologic examinations to prove that the pus found
under such circumstances seldom contains living organ-
isms. This observation has been demonstrated in my
clinic in a large number of instances, in which no
growths were obtained on the culture media, and the
fact that the micro-organisms are dead undoubtedly
plays a large part in contributing to the favorable re-
sults which often follow operative procedures. There is
another point of interest connected with the treatment
advisable in these cases, namely, the influence of the
employment of palliative measures to the acute stages of
purulent invasions of the Fallopian tubes and ovaries.
I have long been convinced that it is an unwise routine

to proceed at once to radical steps during an acute attack
of pelvic abscess. Even if the patient does not improve
somewhat in a short time under general hygienic meas-
ures and external applications together with the exhibi-
tion of suitable drugs, by simply opening up the cul-de-
sac, in the great majority of instances the pus can be
given an outlet through this channel, and the absorption
of the toxic substances present in the pelvis can be
diminished so that as a result the patient's condition will
generally become better. She will then be able to with-
stand the shock if it should later become necessary to
institute radical abdominal measures for the removal of
the pus-sac contents. After having tried this plan of
treatment in a considerable number of cases, and com-
paring the results with those following immediate radi-
cal operative procedures during the acute stage of pelvic
abscess, I have become convinced of the great ad-
vantages of the former method in the majority of
instances.

The micro-organisms that are most frequently met
with in cases of suppurative disease of the Fallopian
tubes and ovaries are *Staphylococcus pyogenes aureus,*
*Streptococcus pyogenes, Gonococcus* and *B. coli.*
Other forms are occasionally met with, such as *B. tuber-*
*culosis,*[1] *Proteus zenkeri.* Of these organisms the one
which is the most to be feared is undoubtedly *Strepto-*
*coccus pyogenes.* But although its presence always
makes the prognosis grave, it must be borne in mind
that there are many instances on record in which this
organism has been found during abdominal operations,
and yet the patient has recovered. This favorable out-
come is to be explained by the wide range of virulence
possessed by *Streptococcus pyogenes.* In my experience
a fatal peritonitis has sometimes followed operative pro-
cedures in which there were no macroscopic evidences of
pus at the time of the operation, and I am inclined to be-
lieve that in such cases, with adherent lateral structures,
the prognosis is often worse than when a considerable
quantity of pus is met with. For this reason, and also
because one can never be absolutely sure that the organ-
ism may not be very virulent, I have for a long time
followed the rule of not performing more than one
abdominal section on the same day, preferring to have
more frequent sessions rather than to run risks. When-
ever I find pus I always postpone carrying out any fur-

1. Recently my assistant, Dr. Howard H. Dittrick, has been able
to grow the tubercle bacillus from the pus of a tuberculous sal-
pingitis.

ther abdominal work, except in emergencies, until 48 hours have elapsed.

*Drainage.*—The question of drainage in pus cases is always of great interest, and all operators are by no means in agreement as to its advantages and disadvantages. In my clinic we have not used a drainage tube during the past seven years, and we now, even in pus cases, seldom drain through the abdominal incision. When should we and when should we not carry out drainage in pus operations? As has already been suggested, the pus that is found in the Fallopian tube and ovary is in the great majority of instances sterile, and if this is the case, what advantage is to be obtained by the use of drainage? Again, if the pus encountered in a given case contains virulent organisms, will the use of drainage prevent a spread of the infection after a complete operation? After a thorough trial of both procedures, I have been forced to the conclusion that no form of drainage will prevent the occurrence of a certain amount of peritonitis if the organism present is virulent. There is, however, a class of cases in which drainage may possibly be indicated, namely, those in which it has been impossible to remove the adherent pus sac or structures completely. In these instances we employ for the purpose gauze sponges, which are introduced through the abdominal incision and carried out through the vagina. If the operation has lasted for a considerable length of time and the patient has been in a more or less marked condition of chronic sepsis, the drainage is kept up for from 24 to 48 hours. I must say, however, that I do not feel altogether sure that even under these circumstances the procedure is always absolutely called for.

In passing, I might say that the only other cases which in my judgment call for drainage are those in which it has been impossible to control the bleeding that occurs after the separation of dense adhesions, or in which, during the separation of adhesions, a rupture of the bowel has taken place, and it has been an exceedingly difficult case to close the rent. In the former case the gauze is used more for the purpose of compression, while in the latter it serves to protect the bowel, and should a leakage of the contents take place they can find an avenue of escape by means of the opening made in the cul-de-sac through which the distal end of the gauze sponge is carried into the vagina. On the other hand, if we have not drained and symptoms should arise after an abdominal section, as the result of the absorption of septic material that has been introduced at

the time of the operation, or from remnants of the retained diseased foci, we have plenty of time, as a rule, to reopen the abdomen and wash it out again, and then, if necessary, institute drainage in order to prevent the absorption of more septic material. Such cases are, however, fortunately very rare, and if we employ drainage as a routine in order to anticipate such a condition we may run many risks of infecting the patient.

### THE TECHNIC TO BE EMPLOYED IN PUS OPERATIONS.

The technic to be carried out in operations for pus in the pelvis differs somewhat from that carried out in ordinary abdominal operations, and although the pus met with under these circumstances is, as a rule, sterile, practical experience has shown it to be a wise precaution to protect as far as possible from infection the portions of the pelvic contents which are apparently intact. In order, therefore, to limit the free distribution of noxious material throughout the abdominal cavity, it is our practice, as soon as the abdomen has been opened, to place large gauze sponges high up in the flanks on either side. If during our manipulations a pus sac is ruptured, we at once lower the patient and then make coverslips of the escaped pus, and, while these are being examined by an assistant, we try to remove as much as possible by mopping it up with gauze sponges. The pelvic cavity is then irrigated with large quantities of sterile salt solution in order to get rid of the greater part of the septic material and to dilute thoroughly any that may still be left. The enucleated mass is now surrounded with gauze which has been moistened in a solution of 1-1000 warm bichlorid of mercury. This gauze is not removed, if it can possibly be kept in place, until the structures have been cut away. If we unexpectedly encounter a pus sac before we have had an opportunity of applying our gauze protection pads, and if the contents escape into the pelvic cavity, the patient is at once lowered to the horizontal posture, and the pelvic and abdominal cavities are irrigated with hot sterile salt solution. The excess having been sponged out and the gauze protection pads placed in position, we then proceed with the enucleation of the mass. The pedicle is thoroughly cauterized with the Paquelin cautery, the abdomen is again washed out with salt solution and sponged dry, after which 300 to 500 c.c. of warm sterile salt solution are introduced and left in the cavity. The incision is closed without drainage. For 24 hours following the operation the lower end of the bed is elevated.

The situation of the pus in this series of 100 cases,

the number of cases in which we were able to demonstrate organisms, and the classification of these organisms may be of some interest.

The pus was found as follows: In the ovary, unilaterally, 30 times; bilaterally, 6 times, including tuberculous cases. In the tube, unilaterally, 36 times; bilaterally, 52 times, with the tuberculous cases. In the appendix once. In the walls of the uterus, once. In almost every case in which the pus was unilateral the tube and ovary on the other side were found to be adherent. Infection of the tube and ovary together (tubo-ovarian abscess) was noted, unilaterally, 21 times, and bilaterally twice. The tubes were more liable to a bilateral infection; the ovaries, to a unilateral infection.

In the tubes and ovaries the following organisms were found: *Staphylococcus pyogenes aureus*, 3 cases; *Staphylococcus pyogenes albus*, 3 cases; *B. coli communis*, 4 cases; *Streptococcus pyogenes*, 4 cases; *Friedländer's bacillus*, 2 cases; *B. tuberculosis*, 2 cases; *Gonococcus*, 8 times positive (six others probable). Thus in 24 cases (24 per cent.) organisms were found.

We were not able to cultivate the gonococcus, except in one instance, and the diagnosis was made in the other cases entirely from the coverslip examinations of sections made from the tissues.

In the two cases in this series which terminated fatally, we had to deal with a streptococcus infection, as was demonstrated by the growth on culture media. In the first case there was a previous history of infection following a miscarriage which had occurred ten weeks before the patient was admitted to the hospital. At the time of the operation we were not able to demonstrate by coverslip examination any organisms in the pus that escaped. No drainage was employed. The infectious material may possibly have been introduced at the time of the operation, although it is quite likely that the process dated from the time of the miscarriage. In the second case the coverslip examination of the pus revealed no organisms, but on tubes inoculated from the pus streptococci were found. The abdomen was reopened on the second day after the operation under cocain anesthesia and washed out, drainage being afterwards instituted. The patient died on the third day. Cultures made from the lung at autopsy showed *Diplococcus pneumoniæ* and *B. coli communis;* in the liver, *B. mucosus capsulatus* was found, and in the peritoneum *Diplococcus pneumoniæ*. In this case, then, streptococci, though not demonstrable by coverslip examinations at

the time of the operation, appeared in the culture tubes two days later. At the time of the autopsy only *Diplococcus pneumoniæ* was found in the peritoneal cavity.

### CONCLUSIONS.

A careful analysis of this series, therefore, seems to justify the following conclusions:

1. The mortality following operations for suppurative diseases of the tubes and ovaries can be kept under 5 per cent.

2. The death rate is largely influenced by *a*, the virulence of the specific organisms present; *b*, the individual resistance of the patient; *c*, the time and manner of carrying out the operative technic.

3. The micro-organism most to be feared is *Streptococcus pyogenes,* but it must be borne in mind that this organism varies considerably in virulence.

4. Abdominal drainage following operations for pus in the tubes and ovaries is seldom called for, as the organisms are generally dead. Drainage becomes necessary only when it has been found impossible to remove the suppurative structures, or where perforation of the bowel from the separation of dense adhesions is to be feared. Under these circumstances the best route is by the vagina.

5. The employment of sterile salt solution for irrigating the pelvic cavity will satisfactorily remove the pus or its products and the filling of the abdomen with salt solution will dilute and promote the rapid absorption of any inflammatory products that may be left behind.

6. The elevated position for 24 hours following the operation, with the abdomen filled with salt solution, tends to prevent the intestines and omentum from coming in contact with the immediate field of operation, and as a result adhesions are not so likely to form between the viscera and the incised surfaces.

7. Should symptoms of infection follow the closing of the wound in pus cases, we have, as a rule, sufficient time to reopen the abdomen and wash out the infective material that may have been left behind, or that may have been introduced at the time of the operation.

8. Operations for pus in the tubes and ovaries from the standpoint of the pus *per se* are not surrounded by more danger, as a rule, than those in which a purulent focus is not present.

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# THE VAGINAL INCISION IN SEPSIS FOLLOWING ABORTION.*

## By Hunter Robb, M.D.,

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I believe that statistics justify the two following statements: (1) Of all married women who die between the ages of 20 and 40 nearly 10 per cent succumb to a puerperal infection; (2) At the present day, in private practice at least, the mortality from child-bed fever is nearly as high as it was 40 years ago. Such a confession is at once astounding and humiliating, and we must of necessity come to the conclusion that the advantages of aseptic and antiseptic procedures are either chimerical or that the belief in them is still to a large extent more theoretical than practical.

But if the mortality is still as high, what shall we say of the morbidity? No reliable statistics dealing with this subject are at hand, and how many cases of septic infection are still classed as instances of milk fever, malaria, nervous chills and the like, remains uncertain. Again it would appear that criminal abortion is very widely practiced at the present day, and certainly it is a matter of surprise that the gross ignorance and recklessness of those who carry out such unlawful procedures do not lead to consequences even more disastrous than those of which we have cognizance. Hence we may conclude that even although every reputable physician should observe the strictest asepsis and that as a consequence child-bed fever should occur only as a rare accident in his practice, there will always remain a number of cases of sepsis after abortion for which the medical profession is in no way responsible but which, nevertheless, it will certainly be called upon to treat.

But even if the unfortunate patient survives an infection following labor or an abortion, she often remains a wretched invalid, sometimes for the rest of her life, or at other times until her sufferings are removed or palliated by a mutilating operation. It can hardly be doubted that fatal or bad later results are often due to an imperfect or an improper treatment of the condition. It is now a generally accepted fact that shortly after the idea of antisepsis had been promulgated, many patients died from sublimate or carbolic-acid poisoning following intra-uterine injections of solutions of these drugs. As a result, such

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*Read before the Cleveland Academy of Medicine, Apr. 17, 1903.

strenuous procedures fell out of favor, especially after experience
had shown that quite a considerable proportion of puerperal, even of
streptococcic, infections will recover, if the patients receive only
symptomatic treatment. Nevertheless, since, as has been pointed out,
such recoveries are often very incomplete, and the patient rarely re-
gains her former health, or at least only after a major operation, it
is our bounden duty always to be on the lookout for some procedure
which may not only reduce the mortality, but may also render re-
covery, when it occurs, more perfect. It is on this subject that I wish
to speak, my remarks dealing mainly with cases of abortion, although
it is not impossible that they may be applicable to a large proportion
of septic cases following labor at term.

So far as my own experience goes, the remote results of a septic
process following labor or an abortion, implicate more particularly the
Fallopian tubes and ovaries in from 40 to 60 per cent of the cases.
When an infection occurs after an abortion, there is usually a chill fol-
lowed by an elevation of temperature, an accelerated pulse rate, and
more or less pain in the lower part of the abdomen. Together with
these symptoms we often have a bloody discharge from the vagina,
or one mixed with pus or mucus, which not infrequently has a very
offensive odor.

As a rule the infection begins in or near the external genitals, and
providing that it is of a virulent nature it implicates successively the
structures of the vagina, the cervix, the uterus and the Fallopian tubes,
and thus extends to the peritoneal cavity. At other times it reaches
the peritoneum through the uterine walls by way of the lymphatics
or blood vessels. Accompanying the inflammation there is often an
exudate, which may accumulate in the peritoneal cavity or may remain
sealed up in the Fallopian tubes. This exudate may be mucous, serous,
purulent or bloody in character; or more often it is of a mixed form.
It may contain virulent organisms, although not infrequently it is
sterile. If the fluid in the cul-de-sac is purulent the Fallopian tubes
and ovaries are very liable to become infected, and the ends of the
former may become sealed up. If absorption of the exudate does not
occur, organization takes place, with the formation of adhesions, which
bind down the tubes and ovaries more or less firmly and thus interfere
with their functions. In this way various symptoms are produced
which cause the patient a greater or less amount of inconvenience
until the adhesions are separated. Under such circumstances we have
two problems to solve. (1) How can we ensure to the patient the

best chance for her life? and (2) How can we at the same time prevent the occurrence of unfortunate sequelæ?

Our present method of dealing with an infection after an abortion is as follows: The cavity of the uterus is first cleaned out in order to prevent the continued absorption of toxines from any infectious material that may be present, and thus at least limit the intensity of the process. For this we employ the finger alone, or combined with the curette. The cavity is then thoroughly washed out with a hot saline solution and two ounces of peroxide of hydrogen; it is then cleansed again with the saline solution and sponged dry. Two or three drachms of iodoform powder are carried into the uterine cavity, after which the latter is packed with strips of sterile gauze. We next make a free opening into the cul-de-sac, and after evacuating any fluid that may be present, we irrigate it freely with hot saline solution, followed by one or two ounces of hydrogen peroxide. After this the cavity is again washed with saline solution and sponged dry. Lastly two or three drachms of sterilized iodoform powder are dusted into the cul-de-sac, which is then packed tightly with strips of sterile gauze. By this procedure we believe that we obtain two distinct advantages: (1) By evacuating the fluid we prevent further absorption of toxines from the cul-de-sac. (2) We save the Fallopian tubes and ovaries by preventing adhesions which would almost inevitably form as a result of the organization of the exudate.

Pryor, of New York, who has written at some length on this subject, does not carry out the vaginal incision unless he can demonstrate the presence of organisms in the uterine cavity. Moreover, even in the latter case, he opens into the cul-de-sac, not for the purpose of drainage, but in order to fill the pelvic cavity with iodoform gauze, whereby he aims at isolating the uterus completely, and bringing all parts of the pelvis into contact with the gauze, which eliminates free iodine when it meets with a serous membrane. Our experience, however, has shown that even when no infective organisms can be demonstrated in the secretions from the uterine cavity, there are not infrequently present in the cul-de-sac purulent or muco-purulent collections containing bacteria. In some of our instances, indeed, a considerable amount of free pus, serum or blood has been found, even when a bimanual examination under full anesthesia had failed to suggest its existence.

I shall briefly present the clinical history with the bacteriologic analysis of 10 cases of sepsis following abortion treated in this way during the past year. The operations were performed by myself and

my assistants at the Lakeside Hospital, and the bacteriologic work was carried out by Dr. Charles D. Williams, my former Resident Gynecologist, in Prof. Howard's Laboratory.

In these cases the results both immediate and later, following the procedure have been so uniformly satisfactory, that we have great hopes that a more extended experience will demonstrate it to be not only a life saving method, but a reliable prophylactic measure against the subsequent loss of function of the lateral structures, and a preventive against much of the wretched health that so many of our patients date from an abortion or a labor.

*Clinical and bacteriologic analysis of ten cases of septic infection following abortion, in which dilatation of the cervix and curetting of the uterine cavity was supplemented by incision into the vaginal cul-de-sac.*

*Age.* The oldest patient was 39, the youngest 19 years of age. The average age was 26 years. Eight were married and 2 were widows.

*Occupation.* Housework, 7; cashier, 1; prostitute, 1.

In 4, full-term births had occurred; there had previously been 11 miscarriages among the 10 patients.

Abortion had been induced in 7 cases, a rubber catheter having been inserted into the uterine cavity.

*Symptoms.* The most frequent symptoms were a sharp or dull pain in the lower abdomen, chills and fever, and a bloody discharge from the vagina.

*Temperature and pulse on admission to hospital.*

The highest temperature was 105.7° F.; highest pulse, 160.

The lowest temperature was 100.3° F.; lowest pulse, 96.

Average maximum temperature 102.7° F.

Average maximum pulse 129.

Lowest maximum temperature 100.3° F.

Lowest maximum pulse 96.

*The vaginal discharge.* In 7, it was bloody in character; in 3, purulent.

*Operation.* In each case the uterine cavity was curetted and the pouch of Douglas was opened.

In 2 cases a slight amount, in 2 cases a large amount and in 6 cases a moderate quantity of débris, was removed from the uterine cavity.

In 3 cases the débris was foul-smelling in character. It consisted of portions of the placenta, fetal tissues and endometrium.

*Material in cul-de-sac.* In 2 cases there was no perceptible amount of fluid in the cul-de-sac and in these cases there was placental tissue in the uterine cavity. In the second case there were cocci on coverslip examination from the cul-de-sac.

In 8 cases in which fluid was found in the cul-de-sac the following amounts and characters were noted:

(1) 800 cc. of sanio-purulent fluid with a fecal odor.

(2) 125 cc. of pus.

(3) A small amount of blood-stained fluid.

(4) About 40 cc. of a clear fluid.

(5) A small amount of clear fluid.

(6) 200 cc. of a purulent fluid.

(7) 70 cc. of pus.

(8) 180 cc. of a sanious fluid.

Thus in 80 per cent of the cases fluid was found in the cul-de-sac varying in amount from a small collection of a clear fluid to 800 cc. of a sanio-purulent fluid. In 4 cases (40 per cent) it was purulent in character.

*Leucocytosis.* In 5 cases in which the blood examination was made, the following counts were recorded: 18,000, 16,000, 12,000, 22,000, 28,000. In the remaining 5 cases the patients were taken to the operating room immediately after admission to the hospital and the blood was not examined.

In 4 of the 5 cases there was a marked increase in the number of the leucocytes.

*Results*—9 recovered, 1 died.

*Coverslip and cultural examination of contents of the uterine cavity and the cul-de-sac.*

Case I. Coverslip:—Numerous cocci and bacilli from the uterine cavity and from the cul-de-sac. Cultures:—B. coli and streptococcus.

Case II. Coverslip:—Negative. Cultures:—Negative.

Case III. Coverslip:—Cocci and bacilli from uterine cavity and from cul-de-sac. Cultures:—B. coli communis.

Case IV. Coverslip from uterine cavity and cul-de-sac:—Negative. Cultures:—Negative.

Case V. Coverslip from uterine cavity and cul-de-sac:—Negative. Cultures:—Negative.

Case VI. Coverslip:—Numerous bacilli from uterine cavity and cul-de-sac. Cultures:—B. coli communis. At autopsy, coverslips from uterus, Fallopian tubes and peritoneal cavity showed strepto-

coccus and B. coli communis. Cultures made at autopsy from Fallopian tubes gave B. coli communis and B. mucosus capsulatus.

Case VII. Coverslips:—No organisms from uterine cavity. Bacilli from cul-de-sac. Cultures:—B. coli communis.

Case VIII. Coverslips:—Uterine cavity negative. Cul-de-sac, Staph. pyogenes albus. Cultures:—Staph. pyogenes albus from cul-de-sac.

Case IX. Coverslips:—Negative from cavity and cul-de-sac. Cultures:—Negative.

Case X. Coverslips:—Cocci from cul-de-sac. Negative from uterine cavity. Cultures:—Negative.

Thus in 5, or 50 per cent, of the cases organisms were found on coverslip and culture-tube examinations.

The following organisms were demonstrated in coverslips and cultures:

B. coli communis, 4 times.

Streptococcus, twice (together with the B. coli).

In one case in which the streptococcus was present it was found in the peritoneal cavity and Fallopian tubes at the autopsy. It was demonstrated only by the coverslip examination.

In 3 cases no organisms were demonstrated either in coverslips or in cultures from the uterine cavity, but in each case organisms were present in the cul-de-sac. In one, B. coli communis and in the other, Staph. pyogenes albus was found, while in the third case no growths could be obtained from the cul-de-sac, although cocci were demonstrable on coverslips.

In 4 cases no organisms could be detected on coverslip or in cultures from the uterine cavity or from the cul-de-sac. In 3 cases the results of the coverslip and culture-tube examinations were similar.

These findings are not altogether in accord with those of certain writers who state that organisms can always be detected in the uterine cavity when the peritoneum is infected. Moreover, our observations show that organisms may be present in the cul-de-sac when none can be detected in the uterine cavity.

The fact that the B. coli communis was the organism present in about 40 per cent. of the cases afforded a more favorable prognosis than would be justifiable in the presence of Streptococcus or Staph. pyogenes aureus. The B. coli communis met with fortunately was not of a high order of virulence.

It may be of interest briefly to detail the history of the fatal case.

*History.* L. Mc. Age 25. Admitted to the hospital, ·July 17, 1902. Married 3 years. Nullipara. One miscarriage at 4 months.

Occupation, housework. On admission she stated that, after missing four menstrual periods, she had had an abortion induced on July 6. Six days later she had chills and fever. The fetus was removed 8 days later by manual manipulation. The fetal sac, however, did not come away at this time. Two days later the patient had a severe chill, followed by a fever and a great deal of pain in the lower abdomen. She was in a marked septic condition; the temperature was 103° F., the pulse 150; she was slightly delirious.

On examination the uterus was found enlarged to about the size of a 5 months' pregnancy. There was a foul-smelling, purulent discharge from the vagina.

She was put under the influence of ether immediately and a large amount of necrotic, foul-smelling material was removed from the uterine cavity by means of the fingers and the curette. The cul-de-sac was incised, allowing from 150 to 180 cc. of a sanio-purulent fluid to escape. The uterine cavity and the cul-de-sac were irrigated with hot salt solution and peroxide of hydrogen, and then sponged dry, after which sterilized iodoform powder, and sterilized gauze were placed in the cul-de-sac. The operation was performed in twenty minutes. The patient soon after went into collapse and died within seven hours.

The following is an abstract of the autopsy protocol (Dr. H. T. Parker) :

"General peritonitis, considerable amount of greenish yellow pus in abdominal cavity. Uterine cavity necrotic and of a blackish green color. This process extends from 1.5 to 2 mm. into the uterine wall. The necrotic surface of the uterine cavity is covered with cocci.

"Coverslips made from the Fallopian tubes, uterine and peritoneal cavities showed streptococcus pyogenes with a bacillus. Culture tubes gave B. coli communis and B. mucosus capsulatus."

In this case, then, we had, as the result of an induced abortion, a general peritonitis, produced by a mixed infection.

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20

## TORSION OF A HYDROSALPINX RESULTING IN INFARCTION.

BY

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TORSION of the Fallopian tube of a grade sufficient to produce pathological changes and marked clinical symptoms is a very uncommon occurrence, especially when the tube alone is affected. The following case, however, presents a typical picture.

N. H., æt. 46, white, married, was admitted to the gynecological service of Lakeside Hospital November 18, 1899, suffering from severe pain in the right side and lower abdomen, which began suddenly the day before admission; nausea, difficulty in micturition, and extreme tenderness in the lower abdomen.

The family history was negative. With the exception of the usual diseases of childhood, patient has always been perfectly healthy and has never had any attacks similar to the present one.

Menstruation began at 16, always regular, and painful before marriage, but not since; duration one week; the last period occurred one week previous to admission. Patient has had two miscarriages, the last twelve years ago, convalescence in both instances being uninterrupted. No viable child has been born. No history of previous pelvic inflammation could be elicited.

Upon examination of the pelvis the uterus was found to be in retroposition, somewhat enlarged, movable and sensitive; the os uteri externum was quite patulous. Apparently in front of the uterus was a rounded, fluctuant, sensitive mass about the size of a baseball; behind and to the right was an ill-defined, smaller, sensitive mass. A provisional diagnosis of right ovarian cyst was made. The examination was unsatisfactory on account of the extreme sensitiveness of the parts.

The temperature on admission was 100° F., pulse 100, respiration 24. The urine showed a trace of albumin with a few hyaline and granular casts. The patient presented symptoms of a localized peritonitis, which subsided under palliative treatment. On November 23, five days after admission, abdominal section was performed by Dr. Hunter Robb. The examination under anesthesia just before operation showed that the uterus was of moderate size and movable; the fundus was directed forward and toward the right side; to the right of the uterus, and movable independently of it, was a fluctuant mass, the size of an orange, suggesting an ovarian cyst. The left ovary seemed small and movable.

An incision was made in the median line and an adherent hematosalpinx, the size of the closed fist and blackish red in color, was found on the right side of the pelvis. The pedicle formed by the mesosalpinx showed two complete twists. The ovary was adherent, but was otherwise unaffected. The adhesions having been separated, the tube and ovary were ligated with silk; they were then removed and the pedicle was cauterized; the left tube and ovary, which were quite adherent, were removed in a similar manner. A small myoma the size of a hazel-nut, attached by a short pedicle to the posterior surface of the fundus upon the left side, was removed by myomectomy, and the incision in the uterus was closed with catgut. The appendix was found bound down by adhesions to the cecum, so that no meso-appendix was apparent. It was therefore removed and the cauterized pedicle covered with peritoneum. The abdomen was flushed out with salt solution and sponged dry, no oozing occurring. Five hundred cubic centimetres of sterile salt solution having been left in the cavity, the abdomen was closed, catgut being used for the peritoneum and the skin and silver wire for the fascia. Convalescence was uninterrupted, the highest temperature being 101.2° F., highest pulse 126. The bowels were opened thoroughly on the day after operation; the dressing was removed on the tenth day, when perfect union was found to have occurred.

Since the patient left the hospital attempts to reach her by letter have been unsuccessful.

*Pathological Examination.*[1]—The *right tube* is occluded at the fimbriated extremity and forms a thin-walled, distended sac containing a thin, bloody fluid. The tube measures 24 centimetres in length around its convexity and 5 centimetres in its greatest

[1] From the Pathological Laboratory of the Lakeside Hospital.

diameter; the weight of the tube and ovary together is 160 grammes; in color it is dark red, almost black in places, and upon the surface there are a number of separated adhesions. The twists formed at the cornual end of the tube were straightened out at the operation. After being hardened in formalin for twenty-four hours, the tube, when cut open longitudinally, shows some half-dozen compartments, increasing in size from the cornual end outward and separated by incomplete septa. Along the sides of the compartments can be recognized the atrophied folds of the mucosa running in a longitudinal direction. The fluid contained in the cavity has not become hardened, but escapes when the tumor is incised.

Microscopically the whole structure is seen to be the seat of a hemorrhagic infarction, being necrotic and infiltrated with red blood cells.

The folds are few in number and scarcely recognizable. A small amount of the epithelial covering is found, the cells being irregular, flattened, and degenerated, being arranged in a single layer. The connective tissue of the folds is crowded with red blood cells, only a few nuclei of the original structure being seen. The muscularis is also infiltrated with red blood cells, the greater part of the muscle either staining very faintly or not at all; around the periphery, however, the nuclei show up more distinctly. The vessels are distended with blood, and the walls are often degenerated. No peritoneal cells are found.

That a distended hydrosalpinx had existed previously to the twisting of the pedicle and the resulting local peritonitis seems highly probable from the complete and evidently long-existing closure of the fimbriated extremity, the atrophic condition of the folds of the mucosa, and the chronic appearance of the septa dividing the lumen into compartments. A further proof of this is to be found in the fact that the contained fluid did not coagulate when subjected to formalin, as would probably have happened if it had consisted of a large proportion of blood or serum, whereas the fluid in most cases of chronic hydrosalpinx fails to coagulate in this hardening agent. Furthermore, it is extremely improbable that a small occluded tube would become twisted, such an accident occurring almost always in cases of tumors of considerable size with a small pedicle such as would accompany a distended hydrosalpinx.

The *right ovary,* measuring 3.5 x 2 x 1.5 centimetres in its various diameters, shows a few slight adhesions, but otherwise ap-

pears normal. Microscopically a few peri-oöphoritic adhesions are seen.

The *left ovary* and *tube* show a number of separated adhesions. Microscopically the tube presents a "healed salpingitis." The appendix, 9 centimetres in length, microscopically appears normal. The small myoma, 2 x 15 x 1.5 centimetres, presents the usual gross and microscopic appearances.

In the literature a considerable number of cases are found; about thirty have been reported altogether. Forselles[1] describes a case of his own and gives an abstract of fourteen other cases reported by as many writers in the literature. Hartman and Raymond[2] report two cases, and, in addition to giving some references found in Forselles' article, quote from five other writers who have met with this condition. In a subsequent article Hartman reports three more cases. Legue[3] describes three cases, one of which had been previously reported; to this reference had also been made by Hartman and Raymond. Ries[4] met with a case of spontaneous amputation of both tubes; later the hydrosalpinx which had formed upon the right side became twisted and infarcted, producing the characteristic symptoms; he refers to an article by Präger[5] in which a number of cases are described. Montgomery also reported a case before the Philadelphia Obstetrical Society.

From the data supplied by the literature the following conclusions may be drawn: This accident, in almost every instance, is found in organs the seat of previous pathological change, the most common condition being a hydrosalpinx. Its occurrence may be explained by the fact that in these cases the tube walls are usually thin, the cornual extremity is narrow, while the fimbriated end is enlarged and distended with fluid, heavy, and is apt to be free from dense adhesions, a considerable range of mobility usually existing. On the other hand, a pyosalpinx is almost always densely adherent, the walls are more thickened and rigid than in a hydrosalpinx, and, the mobility being quite limited, the torsion less frequently occurs. Two or three instances, however, are on record. Torsion of the tube has also

[1] Forselles: Ueber Axendrehung der Tube. Deutsche Zeitschrift für Chirurgie, 1898.

[2] Hartman et Raymond: Le torsion de pedicule des salpingo-ovarites. Annales de Gyn. et d'Obstét., 1898.

[3] Legue: La torsion de salpingitis. Presse méd., Jan., 1900.

[4] Ries: American Gyn. and Obstet. Journal, April, 1900.

[5] Präger: Arch. für Gyn., vol. lviii.

occurred in connection with tubal pregnancy, hematosalpinx, uterine fibroid, parovarian cyst, and hydatid cyst. The tube may also be included in the twisted pedicle of an ovarian cyst, as had happened in the case of a patient upon whom I operated in July, 1899. In two instances the tubes were the seat of malignant disease, and in one case (Hartman and Raymond), occurring during pregnancy, the tubes had evidently been previously healthy. This last is the only instance in which evidences of previous lesions were not found.

The tube alone may be involved, or the ovary may also be included in the torsion. The direction of the twist is inconstant, but usually seems to follow the hands of a watch; the number of twists varies from one-half to four and a half complete turns. In size the tumor may be as large as the fetal head at six months, while in form it is variable, being usually somewhat globular and readily mistaken for an ovarian cyst. The wall is usually thin and the tension rather high.

The pathological changes depend upon the degree of constriction. In one of Legue's cases the pedicle was twisted one and a half times and yet there was no apparent compression or strangulation, although the symptoms were well marked. The first change produced by the torsion will be a venous stasis associated with edema and later with interstitial hemorrhage. In appearance a twisted hydrosalpinx in this condition closely resembles that of an incarcerated intestine, being tense, lustreless, and plum-colored or black. In fact, on several occasions it has been mistaken for the strangulated gut. The later effects would be thrombosis of the vessels with the degenerative changes described by Sänger as hemorrhagic necrosis and by Rundl as a hemorrhagic infarct. Actual necrosis is usually, however, prevented by the formation of adhesions in the less severe cases, while operative measures are, as a rule, carried out in the more grave cases owing to the severity of the symptoms.

The symptoms are practically identical with those arising from a twisted ovarian cyst, and it is often impossible to differentiate between the two until the abdomen is opened. At the site of the lesion there is usually sudden sharp pain, which may be so severe as to cause fainting or collapse. Vomiting may occur, and, in connection with the abdominal pain, may suggest intestinal obstruction or appendicitis, but it does not persist or become fecal. There is rarely obstipation and the temperature is normal or only slightly elevated. A history of one or more previous

attacks may often be obtained, as in torsion of an ovarian cyst.
Upon examination the tense, fluctuating pelvic tumor can usu-
ally be detected; the mobility is often considerable, and in most
of the cases a diagnosis of ovarian cyst with torsion of the
pedicle has been made.

The prognosis is usually good if proper operative measures
can be carried out; the occurrence of a lesion in a pyosalpinx of
course adds to the gravity of the case.

The treatment is operative, and, as many of these patients have
had previous attacks, if the condition seems to be improving it
would seem advisable to wait until the acute attack subsides.

702 ROSE BUILDING.

# RUPTURE OF THE POSTERIOR WALL OF THE CERVIX UTERI WITHOUT INVOLVEMENT OF THE EXTERNAL OS, OCCURRING DURING ABORTION AT THE FOURTH MONTH; ESCAPE OF THE FETUS THROUGH THE LACERATION.

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Lacerations of the cervix, resulting from labor or abortion, usually extend upward from the os externum; they occur on one or both sides of the cervix or they may be multiple; they vary greatly in extent, from a slight fissure to a deep tear, extending up into the vault of the vagina, opening up the parametric tissue or even communicating with the peritoneal cavity.

Tears of the upper part of the cervix not involving the external os are generally due to a rupture of the uterus below the "contraction ring" of Bandl. They may communicate with the abdominal cavity or merely with the parametric tissue. Again, as in the case reported here, the laceration may open into the vagina without implicating either the vaginal vault or the os externum. The only other instance of this sort that I have been able to find is one seen by Gebhard (*Path. Anatomie der Weibliche Sexualorgane,* 1899), in a woman who had died from heart disease just after an abortion at the fifth month. In his case, there was found in the posterior wall of the cervix a large rupture communicating with the cervical canal but not implicating the external os, the latter being quite small and admitting only the finger tip. The abortion had occurred through this tear in the cervix.

Complete separation of the lower border of the cervix, in the form of a circular strip of tissue around the external os, has been mentioned by Winckel. Complete separation of the cervix from the body of the uterus has resulted also from high circular rupture of the uterus, the peritoneal cavity being opened.

Fistulous openings through the anterior cervical wall may result from necrosis induced by long continued pressure of the fetal head against the pubic bone but this accident is of a different nature from

the ordinary lacerations, which are caused by the forcing down of the fetus against a rigid or insufficiently dilated cervix.

The patient, aet. 21, was admitted to the gynecologic service of Lakeside Hospital, May 14, 1900. She presented symptoms of an impending abortion—severe bearing down pains and uterine hemorrhage. Examination showed that the cervix was small and hard and



Fig. 1.　Exposure of posterior surface of Cervix: shows ragged tear in posterior lip of cervix, through which abortion occurred.

the external os contracted and rigid; the uterus was the size of that of a four months' pregnancy; the breasts were somewhat enlarged and colostrum could be squeezed from the nipples.

Three and one-half months previously the menstrual period had not begun when expected and the patient, fearing that she might be pregnant, had inserted a rubber catheter into the uterus. Nothing resulted from this procedure until three days later when she had apparently a normal period. The next menstrual flow also appeared and

vaginal examination after it had ceased did not suggest pregnancy, the cervix being quite hard and small and the uterus but slightly enlarged. A third menstrual period also occurred and a week later the present symptoms began spontaneously.

Abortion being considered inevitable it was decided to hasten matters by dilating the rigid cervix. This was attempted with the Goodell-Ellinger dilator, under cocain anesthesia, but the resistance of the tissues was so great that the canal could not be stretched to more than 1 cm. in diameter. The procedure was executed with the utmost care, apparently without causing the slightest laceration. The patient's condition being excellent, it was decided to await further dilatation by the natural process and a small strip of gauze was left in the cervical canal. During the afternoon the pains were frequent and severe, bromide of potassium and chloral being given without much effect. In the evening the gauze was removed in order to relieve the pain and the cervix was found still rigid and admitting only the tip of the index finger. The pains continued during the night and early on the next morning a four months' fetus within the unruptured amniotic sac and the placenta were expelled. On vaginal examination, made shortly afterward, the external os was found unruptured and surprisingly small; the uterus was contracting well and there was no hemorrhage. No unfavorable symptoms having developed, further examination was postponed until three days later, when a large oval laceration was discovered in the posterior wall of the cervix about 1 cm. above the margin of the external os, involving neither the os nor the vaginal vault. This tear communicated with the cervical canal and had served for the passage of the fetus. It had been entirely overlooked at the first examination.

The opening was sutured with silk-worm gut and excellent union occurred. The convalescence was uninterrupted and the patient's subsequent health has been perfect.

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## CONSERVATISM IN PELVIC SURGERY.[1]

BY

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A THOUGHTFUL conservatism in operative procedures, when
dealing with pathological conditions of the female organs of
generation, has fortunately become the rule in the majority of
surgical clinics. And more particularly is this likely to be the
practice where the surgeon in charge has kept in touch with the
progress that has been made from this standpoint, and from his
own experience and that of others has learned to appreciate the
advantages of conservative procedures in the treatment of pelvic
inflammatory disease. ' There still remain, however, operators
who believe it to be their duty to resort to extreme measures
when dealing with pathological conditions of the tubes and
ovaries, although the same men often favor more conservative
procedures when they encounter general surgical abnormalities.
Now, with few exceptions, the so-called cystic or cirrhotic ovary
is still capable of performing its functions, and when the organ
is bound down by adhesions, the symptoms are apt to be due
mainly to their presence. Hence, in the restricted sense of the
term, the condition of such organs is not pathological, and when
they have been removed under these circumstances they seldom, if
ever, show any evidences of inflammation even upon microscopical
examination.

But even when the ovaries or tubes have undergone actual in-
flammatory changes, or where they are occupied by tumor for-
mations, or are bound down by adhesions so that their func-
tions are interfered with and the necessity for operative pro-
cedures becomes imperative, we still have to decide how far we
ought to go and how we can get the best results for the patient
not only immediately but later on. After an experience of more
than five years in the application of conservative measures in vari-

[1]Read before the Ohio State Medical Society at Cleveland, May 18th,
1904.

were 48; one was 49; one was 50; two were 52. The majority of
the patients were between 17 and 30 years of age.

*Menstrual History.*—The menstrual history was abnormal in
169, and normal in 68 cases. The menopause had taken place in
one. The symptoms presented in the abnormal cases in most in-
stances were those of dysmenorrhea, menorrhagia, prolonged and
irregular flow.

*Leucorrhea.*—One hundred and seventy-six patients gave a his-
tory of a leucorrheal discharge. Of these patients, 124 were mar-
ried, 38 were single, and 14 widowed.

*Married Life.*—165 were married; 52 were single; 20 were
widows. Longest time married, 28 years; shortest time married,
three months. Of the 165 married, 115 had borne children. The
total number of children borne by the 115 patients was 271, the
average being 1.14 per cent. The greatest number of children
borne by one patient was 11. The next greatest number was 9.
Still-born children, 2. Twins, 1. Women having borne one child,
51; 2 children, 21; 3 children, 12; 4 children, 13; 5 children, 4;
6 children, 5; 7 children, 2; 9 children, 2; 11 children, 1.

A history of infection following labor was recorded in 40 cases.
Instrumental delivery was followed by infection in 13 cases. The
total number in which there was a history of infection following
labor, 53.

*Miscarriages.*—Number of patients having had miscarriages,
104; number of miscarriages, 170; married, 83; single, 10; wid-
owed, 10. Abortions or miscarriages had been induced in 52
cases; in the married patients, 34; in single patients, 10; in wid-
ows, 8; patients having had one miscarriage, 65; two miscar-
riages, 22; three miscarriages, 13; four miscarriages, 1; five mis-
carriages, 1; six miscarriages, 1; seven miscarriages, 1. Infection
following a miscarriage had occurred in 42.

*Gonorrheal Infection.*—In 51 patients there was a history of
gonorrheal infection; positive in 32; probable in 19. Of these
28 were married; 19 single, and four widowed.

Among the married the history was positive in 16, probable in
12, and in one was complicated with syphilis.

Among the single the history was positive in 15, and probable
in 4 cases. Among the widows, positive in one case, and prob-
able in three.

A positive history of a specific infection is generally difficult
to obtain, and unless the infection can be surely proven, we are
not justified in making positive deductions from this standpoint.

**It** will be seen from a study of the cases of labors and miscarriages, that infection in these instances plays a very important part in the causation of inflammatory diseases of the tubes and ovaries. Thus, there were 53 cases of infection following labor and 42 following miscarriage—in all 95 cases.

*Bowels.*—In 73 cases there was a history of constipation. Forty-seven of the patients were married; 14 were single; 12 widowed.

*Micturition.*—There was some complaint with this function in 124 cases. Ninety of the patients being married, 23 single; 11 widowed.

*The general condition* was good in 138 cases; in 82 fair; and poor in 17.

*The uterus was adherent* in 121 cases. Eighty-six of the patients were married; 29 single; 6 widowed.

*The bowels were adherent* in 165 cases. One hundred and ten of the patients were married; 42 were single; 13 were widowed.

*The vermiform appendix* was removed in 113 cases. Married, 80; single, 23; widows, 10. In 56 married patients it was adherent; in 14 flexed; in one occluded; in 9 hypertrophied. Single: adherent, 18; flexed, 3; occluded, 1; hypertrophied, 1. Widows: adherent, 8; occluded, 1; hypertrophied, 1.

It was adherent and not removed in two cases on account of an extreme condition of shock after removal of the pelvic structures. One of the patients was married, the other single.

The appendix was adherent in...................... 82 cases
"    "    "   flexed in ...................... 17 "
"    "    "   occluded in .................... 3 "
"    "    "   hypertrophied in ............... 11 "

                 113

STRUCTURES SAVED.

*Ovaries:*

   Right ........................... 93
   Left ........................... 76
   Both (47 times or) ................ 94
   Right (partial) ................... 17
   Left (partial) .................... 17
   Both (partial) ................... 3
   Both ovaries with tubes 17 times or ... 34

              334

This number was saved in 237 cases, a little over one ovary and a third to each patient.

*Tubes:*

|                          |     |
|--------------------------|-----|
| Right ............... | 17  |
| Left ................ | 25  |
| Both 25 times ........ | 50  |
| Right (partial) ...... | 15  |
| Left (partial) ........ | 11  |
| Both (partial)           |     |
| 5 times or .......... | 10  |

Total ............. 128 in 237 cases, or a little more than half a tube to each patient.

### STRUCTURES SAVED IN THE PUS CASES.

Pus was met with in 64 cases out of 237, or in 27.004 per cent. They were divided as follows:

|                                    |     |
|------------------------------------|-----|
| Married ......................... | 36  |
| Single .......................... | 22  |
| Widow ........................... | 6   |
|                                    | 64  |

The pus was found as follows:

*Double pyosalpinx:*

|                          |     |
|--------------------------|-----|
| Married .................... | 22  |
| Single ..................... | 5   |
| Widow ...................... | 3   |
|                          | 30  |

*Single pyosalpinx:*

|                          |     |
|--------------------------|-----|
| Married .................... | 7   |
| Single ..................... | 5   |
| Widow ...................... | 1   |
|                          | 13  |

*Tubo-ovarian abscess with pyosalpinx (single):*

|                          |     |
|--------------------------|-----|
| Married .................... | 6   |
| Single ..................... | 1   |
| Widow ...................... | 0   |
|                          | 7   |

*Tubo-ovarian abscess (double):*

    Married .............................. o

    Single ................................ 8

    Widow ............................... o

                                      ——

                                      8

*Tubo-ovarian abscess (single):*

    Married .............................. 1

    Single ............................... 2

    Widow ............................... 1

                                        ——

                                      4

*Ovarian abscess (double):*

    Married .............................. o

    Single ............................... 1

    Widow ............................... 1

                                        ——

                                      2

#### STRUCTURES SAVED IN PUS CASES.

| *Ovaries.* | | *Tubes.* | |
|---|---|---|---|
| Right ............... | 27 | Right ............... | 5 |
| Left ................ | 15 | Left ................ | 2 |
| Both 12 times, or ...... | 24 | Right (partial) ........ | 2 |
| Right (partial) ....... | 4 | Both (partial) ......... | 2 |
| Left (partial) ........ | 2 | | |
| | —— | | —— |
| | 72 | | 11 |

Thus 72 ovaries were saved in 64 pus cases, or about one and a fifth ovary to each patient. In 12 cases both ovaries were saved. Eleven tubes were saved, or 1 to about every five and a half patients. In these cases the following organisms were found:

                                              *Times.*

Gonococcus ............................. 6

Streptococcus pyogenes .................. 4   (1 doubtful)

Staphy. pyog. aureus .................... 3

Staphy. pyog. albus ..................... 2

B. coli communis ........................ 2

B. mucosus capsulatus ................... 1

Cocci (no growths)...................... 3

                                         ——

                                   21 in all or ⅓ of

                                          the cases.

In the pus cases the abdominal wound became infected 4 times, or 6.25 per cent. From the infected abdominal wounds in the pus cases the following micro-organisms were isolated:

|  | *Times* |
|---|---|
| Streptococci | I |
| B. coli communis | I. |
| Staph. pyog. aureus | I |
| Staph. pyog. albus | I. |
| B. mucosus capsulatus | I |
|  | 5 |

Micro-organisms found in abdominal wounds other than pus cases:

|  | *Times.* |
|---|---|
| B. coli communis | 2 |
| Staphy. pyog. albus | 2 |
| Cocci and bacilli on coverslip, no growth | I |
|  | 5 |

The leucocyte count in the pus cases:

| Highest | 36,000 |
|---|---|
| Lowest | 10,000 |
| Average count | 21.615 |

Drainage was employed in the pus cases as follows:

| Abdominal alone | none |
|---|---|
| Vaginal | 13 times |
| Abdomino-vaginal | 2 " |

Fifteen times, or in 23.43 per cent. of all pus cases.

Drainage was carried out 21 times in 237 cases, or in 8.86 per cent of the total number of cases. Once by the abdomen alone; twice by the abdomen and vagina combined; eighteen times by the vagina alone.

The convalescence was interrupted by the following conditions: Bronchitis in four cases; pneumonia in one case; pleurisy in three cases; phlebitis in one case; abdominal fecal fistula in one; post-operative mania in one; suppuration of abdominal wound twenty times. Total number interrupted, thirty-one.

In those cases interrupted by infection of the abdominal wound (eight of which were in the pus cases), nineteen of the infections were slight and one marked. Total number of abdominal wounds infected, 8.43 per cent. Number of cases requiring a secondary abdominal operation for the relief of symptoms, seven. Number of cases under observation on account of pelvic discomfort, eight. In seven of these cases the symptoms of which the patients complained disappeared after a year's time; one is still complaining. Deaths in the pus cases two, or 3.1 per cent. Deaths in the whole number of cases (237) four, or 1.68 per cent.

CASE I.—Among the pus cases the diplococcus pneumoniæ was found in the secretions in the peritoneal cavity, together with B. mucosus capsulatus and B. coli communis.

CASE II.—The patient also died from the effects of a pelvic peritonitis; autopsy not allowed.

The two remaining cases were in the non-suppurating class.

In one there was an ectopic gestation which had involved the right tube. On the eleventh day following the operation she developed an acute obstruction of the bowels. The temperature and pulse were practically normal. The abdomen was reopened and the obstruction relieved, but she succumbed from shock one hour following the operation. In the second case the disease of the lateral structures was complicated by an adherent, much thickened and contracted gall-bladder, which contained three good-sized gall-stones. The opening made into the gall-bladder was difficult to close. The patient developed a localized peritonitis, which resulted fatally five days after the operation.

702 ROSE BUILDING.

# THE STREPTOCOCCUS IN GYNECOLOGICAL SURGERY.[1]

. BY

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AND

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BACTERIOLOGISTS have still much to learn and teach us about
the streptococcus, especially with reference to the differentiation
of this organism into distinct species or varieties. Clinically,
however, we know a good deal about this organism, and experi-
ence has taught us to regard its capacities for evil with respect
not altogether unmingled with a wholesome dread. We know
that the streptococcus in some form or other is the pathogenic
agent in erysipelas, acute septicemia, the puerperal fevers and
post-operative peritonitides, and thus far researches have taught
us to wonder not so much at the frequency, but rather at the rela-
tive infrequency of acute processes due to the agency of the strep-
tococcus pyogenes. Döderlein has shown that of the vaginal
secretions taken from about 200 cases, nearly 100 were found to
be abnormal, and that 10 per cent. of these pathological secretions
contained the streptococcus pyogenes, which in 50 per cent. of the
cases at least was pathogenic for animals. Under these cir-
cumstances when we remember the bruised and lacerated con-
dition of the genitalia after labor, which would naturally offer
easy access to invading organisms, it would seem surprising that
puerperal infections are not much more common. Czerniewski
found streptococci in the lochia of 33 out of 81 women suffering
from puerperal fever, whereas in those from 57 healthy women
he was able to find this organism only once. In ten fatal cases
he demonstrated its presence in the various organs of the body
after death.

On the other hand, Pryor reports 36 recoveries in 37 cases of

[1] Read before the American Gynecological Society, May, 1904.

puerperal sepsis from which the streptococcus pyogenes was isolated, but attributes his good results to the effects of the iodine which was set free from the iodoform gauze employed by him. Unfortunately our own experience is far less encouraging, and after carefully explaining errors in technique, we have been forced to the conclusion that the organism with which Pryor had to deal was either less virulent than the form encountered by us, or that his patients had more resistance—or that his good results were possibly due to a combination of these two factors.

In order to arrive at some definite conclusions with reference to the streptococcus pyogenes as a cause of death in our own work, we have made an analysis of all our cases in which this organism has been found during the past six years. It will be shown from our observations that quite a large number of our patients died, and one was unimproved. It will also be noticed that in the great majority of cases in which this organism was met with, there was a previous history of infection following labor, or an induced criminal abortion.

In the analysis of all cases the points noted were as follows: Name; age; condition; occupation of the patient; number of children and ages; miscarriages; most frequent symptoms; temperature and pulse on admission; highest temperature; highest pulse; lowest temperature; lowest pulse; average maximum temperature; average maximum pulse; lowest maximum temperature; lowest maximum pulse; leucocytes; operation; results; urinalysis; drainage; condition of the appendix; suppuration; class according to the operation.

*Abortion Cases* (including a few cases of labor after which treatment was necessary):

Total number of cases................................... 137
Average maximum temperature......................100.8° F.
Average maximum pulse................................ 114

### Operations.

Abdominal and vaginal.................................  3
D. & C. with irrigation................................. 71
D. & C. with irrigation and vaginal puncture............... 29
D. & C. (following labor with irrigations)................  2
D. & C., vaginal puncture and irrigation (following labor)...  3
Pelvic abscess; vaginal puncture.........................  1
Miscellaneous operations...............................  6
No operative procedure................................. 12

Abortions completed in hospital $\left\{ \begin{array}{l} \text{(None streptococcus)} \\ \text{(One died)} \end{array} \right\}$ .. 10

     Recoveries ................104 or 75.9 per cent.
     Improved ................. 17 " 12.4 " "
     Unimproved ............... 1 " .8 " "
     Died ..................... 15 " 10.9 " "

    Operations in the case of the patients who died:

Abdominal and vaginal................................ 2
D. & C. and irrigation................................ 5
D. & C. and irrigation and vaginal puncture............ 5
D. & C. and vaginal puncture (following labor)............ 1
Miscellaneous ....................................... 1
Abortion completed in the hospital...................... 1

                                   —

                                  15

   Streptococcus pyogenes in cases of abortion or following labor:
       Total number of cases.................. 16
       Average maximum temperature...... 101.6° F.
       Average maximum pulse.............. 124

### Operations.

Abdominal and vaginal................................ 3
D. & C., irrigation.................................... 2
D. & C., irrigation, and vaginal puncture................. 6
D. & C. and irrigation (following labor)................. 1
D. & C., irrigation, and vaginal puncture (following labor).. 4

                                   —

                                 16

     Recoveries .............. 4 or 25 per cent.
     Improved ..............3 or 18.75 per cent.
     Deaths ................9 or 56.25 per cent.

    In 16 then, of the 137 cases, the streptococcus was found. The total number of all our cases (from all sources) in which the streptococcus was found is 40. Consequently, those in which this organism was found following an abortion or labor formed 40 per cent. of the total number of streptococcus cases from every source.

### Operations in the Cases which Died.

Abdominal and vaginal................................ 2
D. & C., vaginal puncture and irrigation.................. 4

D. & C. and irrigation (following labor).................. 1

D. & C., irrigation and vaginal puncture (following labor)... 2

Furthermore, we find 5 cases and 1 doubtful case which were operated upon here (abdominal operation) not for abortion, but in which there was a history of a previous abortion or labor followed by chills and fever and other symptoms pointing to infection, mild or otherwise.

Cases in which the streptococcus pyogenes was found (from all sources) :

Total number of cases..................... 40

Average maximum temperature........ 101.2° F.

Average maximum pulse.................. 116

### Operations.

Abdominal operation only.......... 5   } 19; of which 7, or

Abdominal and vaginal........... 14   } 36.8 per cent., died.

D. & C. and irrigation (following abortion) ......................... 2

D. & C., irrigation and vaginal puncture (following abortion) ........... 6   16 cases in which the vagina alone was opened; 6, or 37.5 per cent., of

D. & C., irrigation and vaginal puncture (following labor) .............. 4   the patients died.

D. & C. and irrigation following labor.. 1

Pelvic abscess evacuated by vaginal puncture ..................... 1

Miscellaneous ..................... 7

Recoveries ...... 20 or 50 per cent.

Improved ........ 6 " 15 " "

Deaths .......... 14 " 35 " "

### Operations in the Fatal Cases.

Abdominal operation only............ 4

Abdominal and vaginal............. 3

D. & C., irrigation and vaginal puncture following abortion............... 4

D. & C., irrigation and vaginal puncture following labor.................. 2

D. & C. and irrigation following labor.. 1

Of these 14 deaths in the streptococcus cases, 9, or 64.3 per cent., were in cases following labor or abortion.

We find that in all cases the streptococcus was found alone or in combination in the following order of frequency: (1) Streptococcus alone; (2) Streptococcus and Staphylococcus aureus; (3) Streptococcus, Staphylococcus aureus and B. coli communis. As to the regions from which these organisms were obtained we might say that in all cases (except 3 in which they were found in the vagina), the organisms were obtained from the uterus, the adnexa, the cul-de-sac or from several of these situations. In other words, the organisms were present in places which were admittedly not their normal habitat.

In the past six years we have had 724 abdominal sections with a total of 25 deaths—a mortality of 3.45 per cent. In 7, or 28 per cent. of the deaths, the streptococcus pyogenes was demonstrated.

Number of streptococcus cases in the abdominal sections that
    recovered ........................................ 12
Number of cases operated upon by abdominal section....... 19

Number recovered: 12, or 63.2 per cent., leaving a mortality of 36.8 per cent. for the streptococcus cases in which an abdominal section was carried out.

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$2\,\gamma$

# THE EARLY DIAGNOSIS OF CANCER OF THE FUNDUS, WITH REPORT OF CASES.[1]

BY

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(With three illustrations.)

THE routine examination of uterine curettings will undoubtedly enable us in many instances to make a diagnosis of cancer of the fundus in its very earliest stages, while, at the same time, it will probably demonstrate that cancer of the body of the uterus is of more frequent occurrence than has been generally supposed. The exact ratio between the incidence of cancer of the body of the uterus and that of the cervix has not yet been clearly shown. Tesson, in some recent statistics, found it to be from 1 to 4 in 10. Some authorities give the proportion as 1 in 50. Pozzi, in 214 cases of cancer of the uterus, found only 6 in which the process was confined to the body. Within the past six years we have met with 6 cases of cancer of the fundus in 42 cases of cancer of the uterus, *i.e.*, once in every 7 cases of cancer of the uterus.

Unfortunately, as happens also in cancer of the cervix, we do not often meet with the cases in their incipiency. Clinically there may be few, if any, symptoms of cancer of the body of the uterus, even although the condition may have been present for some time. Hemorrhage is less frequent than in cancer of the cervix, and does not as a rule appear until late in the disease, first, because the increase in the number of blood-vessels is not so great as in cervical growths; and secondly, because the diseased tissue is much better protected from any external injury, being enclosed on all sides by the uterine wall.

In fact there are no pathognomonic symptoms and in many cases the patient appears to be in the best of health. As the disease generally occurs in women between 50 and 60 years of age, we should always be on our guard whenever we meet with a patient who gives a history of a delayed menopause, or with a watery or

[1]Read before the Clinical and Pathological Section of the Cleveland Academy of Medicine, October, 1903.

bloody discharge between the periods, or if after the menopause has been passed at irregular or stated intervals a slight watery or bloody discharge is noticed on her linen.

Provided that cancer of the body is recognized before it becomes macroscopically evident and the uterus can be entirely removed, the prognosis for a permanent cure is good, since extension does not usually take place until late in the disease, and generally is not found in the operable cases. Nevertheless, several cases have been reported in which there was secondary involvement in the tubes and ovaries at a relatively early stage (Ries, Lohlein, Wehmer, Reichel).

In an analysis of 30 cases made by Cullen at the Johns Hopkins Hospital, 20, or 60 per cent., of the patients had remained free from any recurrence after periods of time ranging from 11 months to 6 years. Steinbach reports 23 cases, 13 of the patients remaining well after 3 or 4 years. Winter reports 30 cases, 16 of the patients showed no recurrence after 5 years. Two out of our three patients are still living and well; one two years and one three years after the radical operation.

The association of myomatous disease with adeno-carcinoma of the body of the uterus is not uncommon, inasmuch as myomata are so prevalent. As a rule, however, they are small and of no importance. In some instances they are large enough to produce symptoms that mask the cancerous condition.

The history of our cases, in brief, is as follows:

CASE I.[1]—M. E. D. (patient of Dr. C. M. Hoover, of Alliance, Ohio). Single; age 58; occupation, housework; menstruation be-

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[1] This patient returned June 18, 1904—three years and eight months after the radical operation—complaining of having had some colicky pains in the lower abdomen off and on during the previous three months. In addition to these pains she had had shooting pains in the vagina and rectum. In January, 1904, she noticed the presence of some blood and mucus when the bowels were moved. In other respects she had been feeling very well. On examination the vaginal walls seemed perfectly free everywhere. In the pelvis and just beneath the promontory of the sacrum a rounded, somewhat irregular and rather hard tumor, of the size of a lemon, could be palpated. The tumor mass was firmly attached to the anterior rectal wall at this point. Per rectum the mass could be felt just beneath the mucosa of the bowel. On opening into the cul-de-sac on June 29th the tumor mass was found to have infiltrated the rectal wall to such an extent that a radical operation was contraindicated.

This case demonstrates that although the disease focus was removed while it was apparently confined to the fundus of the uterus, metastases occurred in less than four years.

gan at 12, irregular until about 20; menopause at 48. Leucorrhea slight in amount.

"On admission, Oct. 23, 1900, the following record was made: Has had 'female complaint' for 20 years. One year ago last July (1898) had aching and swelling in lower abdomen. In April had colicky pains and bleeding from the vagina as if she was going to menstruate; this lasted for several weeks; in August, 1900, she had a similar attack and a 'regular hemorrhage.'"

"Her previous and family history is negative. She looks worn; weight 148 pounds; bowels constipated; urination frequent."

*Physical examination of pelvis and abdomen.*—Outlet relaxed: vaginal walls prolapsing. Cervix in axis. Uterus in right lateral flexion, somewhat enlarged, movable. Left ovary cystic, not adherent; right ovary not made out.

The urinary analysis showed a trace of albumin and a few leucocytes before and after operation, but otherwise nothing abnormal. On October 24. curetting was performed; the material removed was more abundant than usual and there was considerable hemorrhage. Malignant disease having been diagnosed by examination of the curettings, on October 30 a vaginal hysterosalpingo-oöphorectomy was performed. The convalescence was uninterrupted, and the patient was discharged from the hospital on November 27, in good health.

*Abstract of pathological report.*—*Curettings.*—These are abundand and present a varying appearance on microscopic examination; some fragments show a very marked glandular hyperplasia, while in others an interstitial endometritis is most marked. Where the former condition prevails the surface epithelium consists of a single layer of tall columnar cells showing cilia in places; the cells are crowded together and form a fairly regular surface, but occasionally small projecting tufts are seen. The glands are enormously increased in number, the interstitial tissue being reduced to a minimum; the size is variable; most of them are small, although a number of large glands with secondary gland formations within them are encountered; the lumina are usually regular in outline and empty, but some contain blood, a clear mucoid secretion or a small amount of debris. The glandular epithelium forms a single layer of tall columnar cells closely crowded and showing frequent karyokinesis. The stroma is small in amount and seems completely crowded out from between many of the glands; it shows considerable cellular infiltration and the vessels are numerous. The appearance of the fragments present a typical pic-

ture of the malignant adenoma as described by Gebhard. Other fragments show only a few atrophic glands lined by normal epithelium, while the stroma is very dense and presents considerable cellular infiltration. Still other fragments show a condition intermediate between these two extremes.

*Diagnosis.*—Adenoma malignum corporis uteri. The uterus measures 7.5 cm. in length, 4 cm. in width at the cornua and 2.75 cm. in thickness; it weighs 38 gm.; the external appearance is normal. On section the cervical canal shows submucous ecchymoses due to the former curetting; the uterine cavity measures 3.5 x 1.75 cm. It is slightly yellowish in color with hemorrhagic areas. Near the fundus on the posterior surface is a small area, 7 cm. in diameter, slightly elevated, granular, showing a few



Fig. 1.

minute, dilated and cystic glands. Lower down on the posterior uterine wall is a second similar area, about 3 cm. in length. The remainder of the uterine cavity is smooth. In the left lateral wall is a small, interstitial myoma, less than 1 cm. in diameter (Fig. 1). The right tube and ovary are normal, except for a few light adhehesions. The left tube and ovary are bound together by adhesions; the tube is thickened and occluded; the ovary is distended by a Graafian follicle cyst the size of a walnut.

*Microscopically* the uterine mucosa is scanty, most of it having been curetted away. When present, it shows a condition similar to that seen in the curettings. Remnants are found on the roughened areas noted macroscopically. The muscularis is normal and is not invaded by the neoplasm. The right tube shows a slight

chronic endosalpingitis with a few surface adhesions. The right ovary presents surface adhesions and the usual senile changes. The left tube is thickened by a diffuse chronic salpingitis. The left ovary shows surface adhesions and a follicular hypertrophy.

CASE II.—J. S. (patient of Dr. Dorman, of Ashtabula, Ohio). Age 40; married for 17 years; II-para, the last labor 8 years ago, the first instrumental; 1 miscarriage 12 years ago. The menses began at 11, regular, occasionally painful, duration one week usually, but of late more profuse and of longer duration; flowing when admitted. Leucorrhea, moderate in amount.

*The present trouble* began about one year ago with profuse menstruation which is becoming more pronounced every month. She has had several severe hemorrhages and on admission had been flowing continuously for 17 days. During the past week she has noticed low down in the right iliac region a tumor as large as an apple; there has been occasional pain in the lower abdomen; the bowels are loose; the patient is anemic, the hemoglobin being 55 per cent. The inguinal glands on the left side are slightly enlarged.

The urine showed a faint trace of albumin before, together with a few hyaline casts after, operation.

*Pelvic examination.*—Outlet relaxed, cervix far back and crosses axis of vagina, moderately deep bilateral laceration. Filling the cervical canal is felt a friable polypus. The uterus is enlarged and irregular in outline, suggesting a myoma. Both ovaries are small and freely movable.

On March 14, patient was curetted, the material being abundant.

On March 20, a combined vaginal and abdominal pan-hysterectomy was performed. Convalescence was uninterrupted except for a brief rise of temperature with slight aphasia for a few days after the operation. The hemoglobin was 75 per cent. when the patient was discharged, April 22, 1901.

*The microscopical examination of the curettings* shows the surface of the cavity to be very irregular, numerous finger-like growths, varying in length and shape, being present. The central stroma of these is somewhat loose and densely infiltrated with leucocytes. The epithelial covering consists of a single layer, or more often of two or more layers. Many of the processes consist of epithelial cells without any stroma. When occurring in a single layer the epithelial cells show elongate oval nuclei, staining fairly uniformly. Hyperchromatic forms are also found. The nuclei of the stratified epithelium vary in size, shape and intensity

of staining; a few very large forms with excess of chromatin oc-
cur; karyokinetic figures are often seen. There is marked leuco-
cytic infiltration of the epithelial covering and degenerated areas
occur in it. The glands are enormously increased in number and
vary from the normal to typically malignant forms. They are
very irregular in size and shape, are often lined by stratified epi-
thelium and present villous-like epithelial tufts, with or without
stroma, extending into the gland lumen and often reaching the
stage of secondary gland formation. Some of the gland spaces
are completely filled with epithelium; others contain desquamated
and degenerated epithelium, leucocytes or a mucinous material.
The epithelium for the most part is pale, swollen and somewhat
degenerated. It is infiltrated with leucocytes and shows a few
karyokinetic figures; in some places the nuclei are very irregular
in size and shape and show an excess of chromatin. The stroma
is fairly abundant, although crowded out from between many of
the glands, it is densely infiltrated with leucocytes, except in the
deeper part. Blood-vessels are very numerous. In places the
tissue is quite necrotic.

　 *Diagnosis.*—Adeno-carcinoma corporis uteri. The tissues re-
moved by hysterectomy consist of the myomatous uterus with
both ovaries and Fallopian tubes. The uterus measures
14 cm. in length, 8 cm. in its antero-posterior di-
ameter, 13 cm. in width at the cornua, 5.5 cm. in width
at the internal os. The peritoneal surface is smooth except near
the left cornu, where a small myomatous nodule, 1.5 cm. in di-
ameter, can be felt in the posterior wall; near it are several small-
er ones the size of peas. The uterine walls are thick and pale,
averaging 3 cm. in thickness; the uterine cavity is 4.6 cm. in
width. In the anterior wall of the uterus and filling the greater
part of its cavity is a myoma 5.5 x 4.4 cm., partly submucous and
partly interstitial; its surface is more or less rough, especially
at the upper margin. The tumor is quite firm, except at its lower
part where it is necrotic and yellowish-white in color. The left
side of the uterine cavity extending down to within 1.5 cm. of
the internal os, and part of the anterior wall present numerous
little outgrowths, 2.5 mm. high, separated by furrows or sulci.
They are most in evidence at the left cornu. The growth has in-
vaded the underlying muscularis to a depth of 1 cm. in one place.
The remaining mucosa of the uterine cavity is smooth but some-
what injected near the lower margin of the large myoma; the
mucosa of the cervix is apparently hypertrophied (Fig. 2).

*Microscopically,* the cervix shows a marked interstitial cervicitis. The mucosa of the body, except in the papillary area, is thin; the glands are few in number and lined by normal pale epithelium. The surface epithelium, usually in a single layer of irregular cells, is occasionally stratified, but shows no apparent signs of malignant disease. The stroma shows a marked interstitial endometritis; the papillary area shows typical adeno-carcinoma, the appearance being similar to those described in the curettings. The margin is rather abrupt both in the mucosa and also in the muscularis; the latter shows a slight cellular infiltration



Fig. 2.

before the advancing growth, but at a short distance from it, it is normal. The characteristic feature of the growth is the large number of glands of moderate size and lined by a single layer of epithelium suggesting the malignant adenoma of Gebhard. The large myoma shows more or less complete hyaline degeneration. At its lower border it is quite necrotic with dense leucocytic infiltration.

The right ovary shows a slight oöphoritis and chronic peri-oöphoritis.

The right tube shows an acute catarrhal salpingitis. There is dense cellular infiltration and the lumen contains a small amount of purulent exudate. The left ovary and tube are normal.

CASE III.—J. McG.; age 52; married 26 years; III-para, oldest child 25, youngest 20; 2 miscarriages, last 22 years ago. Patient

well nourished, weighs 165 pounds. The menses began at 13; last regular period 2 years ago.

*Present trouble.*—For the past ten months the patient has had a slight leucorrheal discharge with some odor, and more or less bloody, the color having been brighter of late.

The general physical examination was negative. The urine was normal before operation; afterwards it showed a faint trace of albumin and red and white blood cells.

*Pelvic examination.*—Outlet relaxed; cervix in axis; posterior lip somewhat irregular; uterus sagging in pelvis, somewhat smaller than normal, movable; fundus forward; lateral structures not clearly made out but no adhesions detected.

On June 18 the uterus was curetted and a portion of the cervix was excised for microscopical examination. The curettings were abundant, 15-20 times the normal amount. Anedo-carcinoma was diagnosed from the microscopical examination. Vaginal hysterectomy was performed June 27, 1902. The convalescence was uninterrupted.

The pathological appearance of the curettings varies in the different fragments. As a rule the surface epithelium forms little tufts with or without a stroma basis; the epithelial cells are mostly columnar but some are cuboidal. They vary from two to many layers in thickness; the cells differ in size; the nuclei lack uniformity in size, shape and position within the cell, and the intensity of staining. A formation of new glands from the surface can be seen. Large numbers of leucocytes occupy spaces between the epithelial cells. The glands are very numerous and in some areas completely displace the stroma. They vary in size and shape, some being much hypertrophied and showing secondary glandular formation within their lumina. The glandular epithelium is stratified and often completely fills the cavity; otherwise the lumina are of various sizes and shapes and contain desquamated epithelium, leucocytes and necrotic debris. The epithelium is infiltrated with many leucocytes. The cells vary in size and the nuclei also differ markedly in size and staining qualities; many karyokinetic figures are found. The stroma in the most affected areas is almost completely crowded out by the large masses of epithelium. Elsewhere it is less reduced and shows large numbers of vessels and more or less cellular infiltration.

*Diagnosis.*—Adeno-carcinoma corporis uteri. The uterus removed by vaginal hysterectomy measures 11.5 cm. in length and 8 cm. transversely. At the right cornu a small part of the

tube is found, 3.5 cm. long and .5 cm. in diameter. The cervix appears about normal except for the loss of a wedge of tissue removed for examination at the present operation. The uterine mucosa, about 2 mm. thick, is somewhat injected, but otherwise normal, except for an area about 2.5 cm. in width near the right cornu where a finely lobulated, soft, friable, yellowish-white papillary or cauliflower-like growth is found. This projects above the surrounding level and also hangs downward somewhat like a polyp over the normal mucosa at its lower limits. The



Fig. 3.

growth also invades the muscularis below it, the boundary line between the two being indistinct.

The uterine wall, as a rule, is somewhat thickened, but beneath the neoplasm it is but half as thick as on the opposite side in a similar position. The portion of Fallopian tube seems normal (Fig. 3).

*Microscopically* the cervix uteri shows a slight cervicitis; the endometrium of the corpus, as far as the limits of the polypoid growth, is thin with few glands of normal appearance and with a dense stroma, the surface epithelium being nearly normal. The border of the neoplasm is rather sharply marked. It is a typical adeno-carcinoma, consisting of large glands showing the formation of secondary glands within the main lumina and usually completely filled by the proliferating epithelium. The stroma is scanty and infiltrated with leucocytes, the appearances being similar to

PATHOLOGICAL AND EXPERIMENTAL PAPERS.

# An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations

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## INTRODUCTION

THE several subjects comprising this research were suggested by practical experience in the operating room. As most of our exact knowledge of human functions has been gained by animal experimentation, it would seem to be safe to apply the laws thus obtained to surgical practice. This is more particularly true of the vascular and nervous systems. Upon the ready and the exact application of such laws depend the immediate results of many operations.

This research extended over three years, during which time the results were clinically compared and applied in an active operative practice. It was exceedingly gratifying to note the close correspondence between the phenomena observed in the operating room and in the laboratory.

While surgical anatomy occupies a conspicuous place in literature, surgical physiology, although almost as important, is all but unknown. Unknown, because the physiologic laboratory is a comparatively recent creation, whose important surgical relations are scarcely appreciated.

The experimental data, tracings, specimens, etc., have been preserved, and there is no statement made that may not be verified. A sufficient number of illustrations have been added to elucidate the text. Unless otherwise specified the experiments were made on dogs, taken unselected as they were supplied by the laboratory servant. Every precaution was taken to inflict as little pain or distress as possible.

ON THE EFFECT OF SEVERING AND OF MECHANICALLY IRRITATING
THE VAGI

(The Protocols of the nine experiments on dogs, of which the following is a
summary, are published in the original essay.)

In the dog the sympathetic fibres run in a common trunk with
the vagus proper. Therefore this nerve has been designated the
vago-sympathetic, so that allowance must be made for the
sympathetic factor. Picking up the artery and nerve together
and bringing them up in the wound, making an ordinary blunt
dissection and separating these structures from their surrounding
tissues, produced slight effect upon the circulation and respiration.
On separating the nerve from the artery by means of blunt dis-
section comparatively slight effects were noted. Grasping the
nerve with the forceps produced, in most instances, a rise in the
blood-pressure and a slowing of the respiration. Dragging down
upon the nerve produced a marked effect. Picking up the nerve
and rubbing it up and down, between the fingers, producing as
much irritation as possible, caused a very distinct slowing of the
respiration, and in most instances a rise in the blood-pressure.
Occasionally, however, there would be a temporary fall with a
marked increase of the length of the heart strokes, indicating an
inhibitory effect. In no instance was the heart completeiv
inhibited. Grasping the nerve with two hemostatic forceps and
so manipulating and irritating it, by sliding the forceps up and-
down, as to finally wear the nerve in two, produced in most
instances a rise in the blood-pressure, and usually a very decided
slowing in the respiration. Not only was the respiration slowed,
but the amplitude was diminished. It required some time before
the normal rapidity and the amplitude were regained. No amount
of mechanical irritation, even to the extent of mechanically
destroying the vagi, produced an arrest of the heart's action.
Severing one vagus was attended by comparatively little effect
upon either respiration or circulation. Usually there was a slight
rise in the blood-pressure, and a slight decrease in the frequency
of respiration with an increase in the amplitude. The blood-
pressure curve remained regular, and no particular effect upon
the amplitude of the excursion of the manometer was noted.
However, on severing both vagi the blood-pressure rose con-
siderably, ran an uneven course, the frequency of the heart's
action was much increased and the length of the stroke shortened.
Respirations were greatly decreased in frequency, and the ampli-
tude of the respiratory excursion was markedly increased, so
that, as nearly as could be estimated, the loss occasioned by the
respiratory action was about counterbalanced by the increased

amplitude of the excursion. The respiratory mechanism was much more affected than the circulatory and exhibited early signs of exhaustion.

### CLINICAL OBSERVATIONS

CASE 1: Excision of the right vagus together with all the venous and arterial trunks on that side, in operation for malignant disease; respiratory failure after the operation; recovery.

John W., aged 30 years and 11 months, had had a very large median epithelioma of the lower lip removed. He returned to the hospital because of tumors on both sides of the neck; the glands were extensively involved; those on the left side were removed at a separate operation. The dissection was extensive, involving the removal of the external jugular vein, the external carotid artery, the submaxillary and parotid glands, exposing by close dissection the common carotid artery and the vagus nerve. Two weeks later the right side was operated. A chain of glands along the internal jugular vein was so extensively involved that on reaching this point it was found necessary to sacrifice both jugular veins, the common carotid artery and its branches. The artery was separated from the vagus, but on carrying the dissection higher it was found that the vagus was so directly involved in the growth that it was necessary to sacrifice it. A consultant made a pulse count both before and after severing the nerve. The heart became accelerated four beats per minute. No other effect was noted. Respirations were not affected. A hypodermic injection of 1/100 grain of atropin was previously given. The dissection was then carried up behind the angle of the jaw, including the submaxillary and the parotid glands, the facial artery and nerve, and all the soft parts. The vagus was then severed just below the point at which the superior laryngeal is given off. This nerve and the lingual were laid bare in the dissection. The dissection was carried far behind the angle of the jaw, and the vessels were so deeply severed as to leave an insufficient length for applying a ligature. By means of a small curved needle, armed with silk, the deep structures around these vessels were picked up, forming a close purse-string, which when tied closed them. During the latter part of the operation the respirations were considerably slowed and the patient became somewhat cyanotic. The wound was then closed after completelyarresting the hemorrhage. The sympathetic nerve was laid bare throughout most of its course, the superior cervical ganglion lying upon the floor of the wound was wholly exposed. After closing the wound by bringing together as far as possible its deeper portions by

means of catgut sutures, the patient was sent to the ward. Directly afterward he was reported to be in a critical condition due to respiratory failure. Upon arriving at the bedside, I found the house surgeon maintaining artificial respiration. While observing the patient I noticed fresh blood on the dressings, indicating a dangerous hemorrhage. Hastily cutting away the dressings and laying open the wound, I thrust my hand into the upper angle from which the hemorrhage came. Although this was quickly done there was a great loss of blood. With my hand grasping his throat he was replaced upon the ward ambulance and taken to the operating room, the house surgeon maintaining, as well as he could, artificial respiration on the way. On returning to the operating room the large vessels were clamped and the forceps allowed to remain. The patient was removed from the ward to the operating room on account of want of light. Ice and heat were alternately applied, which helped to restore the respiratory action. He was given subcutaneous injections of saline solution and 1/200 grain of strychnin every half hour. At the end of twenty-four hours the forceps were removed, and at no time after recovery from immediate effects of the operation were there observed any unusual respiratory or circulatory symptoms. Patient made a good recovery. The microscopic examination of the growth showed a large number of inclusion cells, indicating a marked malignancy. There was considerable hoarseness for two weeks, after which it gradually disappeared. The respiratory failure in this case was in full accord with the experimental evidence.

CASE 2 (Abstract): In removing glandular metastases, following total laryngectomy for carcinoma, the left carotid artery and vagus were involved. The pulse and respirations were observed during the excision and after it. A hypodermic injection of 1/100 grain of atropin was given twenty minutes before the operation was begun. The nerve was severed by a quick snip of the scissors. There was some hoarseness for several days, after which it gradually disappeared. No other effects were noted. The patient made a good recovery.

CASE 3: See report under closing the carotid artery. In this patient the vagus was resected. One 1/100 grain of atropin was administered prior to the operation. No immediate effects were noted. The voice could not, for obvious reasons, be observed.

CASE 4 (Abstract): A full charge from a shot gun, whose muzzle was within a few inches of the patient's neck when dis-

charged, entered the neck in the upper part of the carotid triangle. The artery was torn off and the nerve lacerated. The wadding and shot were firmly packed upon and driven into the torn nerve and other structures of the neck. The pulse was reduced to 42 beats per minute. Respirations were slow, exhibiting quickened respiratory action with lengthened pause and prolonged expiratory action. The slow pulse continued more than two hours, after which the "vagal" mechanism went into resolution and an extremely rapid cardiac action followed.

CASE 5 (Abstract): In removing a mixed tumor of the parotid, the dissection was carried for some distance upon the carotid and the vagus. While freeing the nerve near the level of the tip of the styloid process the pulse dropped from 90 to 56. The wound was almost bloodless, exhibiting the various structures in plain sight. A 4% solution of cocain was applied upon a piece of cotton and the dissection carried elsewhere. After three minutes the dissection of the vagus was again resumed. Meanwhile, the pulse had returned to 86. During the remainder of the resection of the vagus there was no appreciable alteration in the heart's action, in spite of a more severe manipulation than had before been given. The depth of the tumor not having been anticipated no atropin had been administered. This case illustrated the effect of stimulation of the upper portion of the vagus, notably near the point at which the superior laryngeal is given off. This nerve trunk, though not seen at the time, might have contributed to the cardiac phenomena from indirect violence.

CASE 6 (Abstract): Emergency removal, without anesthesia, of a large goitre in unconsciousness from asphyxia. Vagus clamped. Recovery.

Preliminary administration of 1/100 grain of atropin; inclusion of vagus nerve in large forceps; no cardiac inhibition; artificial respiration.

Female, aged 64; had had a goitre 12 years, which during the six months preceding the operation had rapidly developed. The tumor was large, quite firm, deeply situated in the neck, extending well down behind the sternum and clavicle, displacing the apex of the lung and producing a compression of the trachea against the vertebral column. The tumor was so firmly fixed as to be scarcely movable. During two months she had been obliged to make use of the extraordinay muscles of respiration. The development of the platysma was remarkable. In each inspiratory effort the contraction of the muscle was so powerful as to draw down the angles of the mouth, lower lip, and the integument of

the lower part of her face, to throw in vertical folds the entire surface of her neck and upper thorax, and to entirely change the aspect of the neck and face. The lower jaw, meanwhile, was carried fixedly forward and upward. By this means she was able to so slightly relieve the pressure upon the trachea as to accomplish a stridulous though scant exchange of air. It was planned to expose the tumor under local anesthesia, then try to relieve the obstruction by elevating the tumor while administering general anesthesia. She was placed upon the table, but was absolutely unable to breathe in a lying posture. She struggled for breath, sprang up in a sitting posture, then gasping, turned cyanotic, became unconscious, and fell apparently lifeless on the table. At a single stroke with a scalpel the tumor was laid bare, then literally torn out, while the blood from the many torn vessels flooded her face and neck. Artificial respiration was in the meantime begun. The hemorrhage was first controlled by firm gauze packing, then with a large forceps the common carotid, jugular vein, and vagus nerve were grasped *en masse* below and likewise above, completely controlling the hemorrhage. The operation was performed in about 45 seconds. The patient had been given 1/100 grain of atropin previous to the operation, which prevented any cardiac inhibition, although the vagus was crushed at the point of clasping. The operation was completed without her knowledge. She said afterwards that she believed she was dying and was conscious that something was done, but had no pain. Patient made a good recovery.

ON THE EFFECT OF INTRAVENOUS INFUSION OF SALINE SOLUTION

SUMMARY OF SIXTY-ONE EXPERIMENTS

*Circulation:* The intravenous injection of saline solution at or near normal temperature into the circulation of the animal from a height producing a pressure greater than that of the blood usually caused a rise in the blood-pressure. The beginning of this rise appeared as soon as the force of the stream was added to that of the circulation. The rise was sometimes abrupt, sometimes gradual, appearing at once or after a lapse of a short time. In almost every instance a point was soon reached above which no amount of saline solution, irrespective of the height to which the bottle was elevated, could raise it. As a rule the increase in the height of the blood-pressure was but slight, varying from two to six or eight millimetres of mercury. The cases in which there was no immediate rise after the beginning of the infusion were mostly those in which there has been some previous alter-

ation in the blood-pressure. In a small number of the experiments there was immediate temporary fall. This was usually rather abrupt, and in every instance a recovery to the previous level was made or the pressure went even higher.

The character of the heart-strokes in many instances was not altered; but in cases in which it was, an increase in the length of the stroke occurred. The frequency of the heart beats was usually diminished. The general characteristics of the blood-pressure appeared from the time at which it reached its maximum height, after the beginning of the flow, to the time when the beginning of the final decline occurred. The curve was remarkably even. If at the beginning of the flow the curve was irregular the saline injection usually prevented its continuation, establishing a mean level. When, as a result of the continuous flow, death was produced by an excessive amount, the beginning of the death phenomena was marked by the gradual decline in the blood-pressure and in no instance was it possible to stop the downward tendency. The heart-beats composing this curve were characterized by their becoming for a time increasingly longer, then gradually shorter, until the last beat. The frequency was generally diminished from the beginning of the final decline, and if, during this descending curve, the animal executed a respiratory movement, even though it were but a gasp, a very marked alteration in the blood-pressure curve was produced, that is to say, the final descending curve presented the essential characteristics of death from asphyxia.

The preceding remarks apply to the experiments in which normal saline solution at the temperature of the body was given to normal animals in a continuous injection until death. If at any time after a sufficient amount of saline had been administered to raise the blood-pressure to the maximum the animal's foot was burned, or other injury inflicted, an additional rise would follow. This rise, however, was not so high as in the cases in which no infusion had been previously given. It was observed that chloroform, even the inhalation of a few drops, caused an immediate but gradual fall in the blood-pressure, in many instances the fall being marked. Ether, as a rule, produced no change upon the blood-pressure. The effect of chloroform was the more marked the greater the amount of saline that had been previously given. As to the effect of administering the saline at different rates of flow, the more rapidly it was introduced, the more quickly the blood-pressure reached the highest point in that particular case, but the final height would be the same. When introduced

with great rapidity the animal, though under full surgical anes-
thesia, would respond in a peculiar subconscious way, showing a
tendency to struggle.

*The Effect upon the Blood Itself:* On making blood-counts
by means of a Thoma-Zeiss instrument before and during the
saline infusion a decrease on the number of red cells was usually
shown. The blood-counts, however, exhibited a great variation
in the different experiments. In two they showed an actual
increase in the number of red cells, but, as a rule, the number
fell, generally about 1/4 to 1/5. The blood-counts, though very
carefully made, in the same experiment at different stages, showed
varying results, and in some instances after considerable diminu-
tion there would be a secondary increase. The blood-count was
not proportional to the amount of infusion. The tendency to clot
seemed to increase with the experiment. This was especially
marked in the blood from the liver. The color of the blood grew
darker from the time of the beginning of the final descent of the
blood-pressure until the end. Earlier its color was a lighter red.
There was a very marked increase in the tendency to hemorrhage,
especially from the small vessels. Wounds made before the intro-
duction of the saline and which had become dry began to ooze
soon after the beginning of the infusion. The temperature in
many instances was slightly raised.

The foregoing applies to a dog under surgical anesthesia
in which normal saline solution at the temperature of the body
was allowed to flow until death occurred.

*On Respiration:* The respirations were increased or dimin-
ished according to the circumstances. If saline was introduced
rapidly the alteration, both as to increase in frequency and in the
amplitude of the stroke, was more decided. This increase did not
continue, but after a period of time, corresponding fairly well
with that allowed for the circulatory changes to reach their maxi-
mum, the respiratory rhythm returned nearly to the normal. As
the animal became increasingly under the effect of the infusion the
respirations decreased in frequency while the amplitude of the
excursions increased. The abdominal factor of respiration grad-
ually diminished until it was lost, and the costal factor alone
assumed the burden. This factor soon began to fail—death ensu-
ing. When once this tendency was inaugurated, it continued until
the end. In every instance after the appearance of these phe-
nomena death ensued. There was not even a temporary improve-
ment. During the latter part of this period the extraordinary
muscles of respiration were brought into action, the respiration

becoming gasping. The respirations always failed before the heart. All the animals died of respiratory failure. The characteristic decline of the blood-pressure curve, referred to under the heading "Effects upon Circulation," were inaugurated after respiration had ceased, *pari passu* with the development of the later saline phenomena. Coarse, moist râles of varying intensity developed. They were first heard most distinctly over the pulmonary bases, then over the entire chest, and later could be heard when standing near the dog-board. During this stage of the experiment dulness over the pulmonary bases developed, extending later over other portions. In the greater number of the experiments the tracheal cannula became filled with fluid having a consistency varying from a tenacious to a watery fluid. Sometimes it seemed to consist of bloody serum, at other times of a frothy mucus. In some instances this fluid collected in such quantities as to materially interfere with the respiratory action, making it necessary to tilt the dog-board and turn out the fluid.

*The Effect upon Tissues and Organs:* There was an increased amount of fluid in the skin. The muscles of the extremities contained a slightly increased amount of fluid and those of the trunk and neck were decidedly more edematous. The connective tissue was more moist than normal and occasionally was emphysematous. The heart was always in diastole, the chambers widely distended and usually filled with clots. No fluid was in the pericardium. The heart muscles were somewhat edematous. The venous trunks were everywhere distended, imparting to the touch the sense of a decidedly increased tension. The smaller veins also were distended, especially the mesenteric and subcutaneous. The capillaries and the smaller vessels of the gastro-intestinal tract almost disappeared. In the lungs, underneath the capsule of the kidney, and in the walls of the stomach there was in many cases capillary hemorrhage. The same was noticed, in some instances, under the coverings of the brain. The arterial system was not distended. The portal circulation was greatly engorged.

*Respiratory Tract: Nose.* The mucous membrane of the nose was edematous and usually bathed in mucus. During the latter stages mucus discharged freely from the nose.

*Trachea.* The mucous membrane of the trachea was edematous, being more or less filled with clear, though more frequently a bloody fluid.

*Lungs.* In almost every instance the lungs were edematous and ecchymosed. The edema and ecchymosis were most marked

in the bases, diminishing over other portions. The ecchymosis varied from small points of a diffused color up to an ecchymosis so intense as to resemble the liver. In some instances the bases were extremely dark, soggy, heavy, and when fragments were thrown into the water they floated very low. On incising them, quantities of frothy, bloody fluid escaped, but in some the fluid was quite clear. Frequently fluid was found in the thoracic cavity. This in many instances was bloody.

*The Alimentary Tract: Mouth.* The mucous membrane was thickened and edematous. There was free discharge from the mouth consisting of a mixture of a watery fluid and mucus. In some instances there was a free discharge of fluid, probably from the stomach.

The pharynx, esophagus and stomach were edematous and the mucous membrane was thickened. The stomach in every instance was much distended with watery fluid. The wall of the stomach was considerably thickened, and at times both the mucous membrane and the serous surfaces were pale, though more frequently white. The wall was so edematous that on incising it its histologic layers were to a considerable extent separated and watery fluid oozed from its cut surface. Its cavity was more or less filled with watery fluid.

*Intestines.* The small intestines were white, their walls much thickened and edematous. On incising them the histologic layers were well separated and fluid oozed from the cut surface. Usually their lumen was filled with watery fluid. The large intestine presented like conditions, decreasing toward the anus. There was free fluid in the peritoneal cavity and in some instances a large quantity. In many of the experiments the intestines were so filled with fluid that it escaped from both the anus and the mouth.

*Liver.* The liver in many instances was hard and greatly enlarged. On making incisions, large quantities of diluted blood escaped, at times spurting. Even when the incision was made at one point the entire liver decreased in size *pari passu* with the flow, and the hardness disappeared.

*Gall Bladder.* The gall bladder was usually filled with bile.

*Spleen.* The spleen usually contained more fluid than normal.

*Pancreas.* The pancreas was in most instances enlarged and edematous.

*Urinary Tract:* The kidneys were but slightly enlarged, and on incising them considerable pale fluid escaped, especially from

the pelvis. Occasionally there was ecchymosis underneath the capsule. The ureters were somewhat enlarged. When the experiment was continued for a length of time the urinary bladder was usually extremely distended, but its walls were not thickened. In shorter experiments there was no distention.

## EXPERIMENTS IN WHICH THE ABDOMINAL AORTA, INCLUDING THE SPLANCHNIC ARTERIES, OR IN WHICH THE LATTER ALONE WERE CLOSED

In this series of experiments, in which either the abdominal aorta or at least some of the splanchnic vessels were closed before the saline solution was allowed to flow, death ensued before an equal relative amount of the solution had been given, that is to say, the normal dog could take much more saline than an animal whose splanchnic area had been excluded by closing the supplying vessels. Pulmonary edema developed. The animals died of respiratory failure, the blood usually became cyanotic. In most cases the heart showed the effect of asphyxia by beating more slowly but very strongly. The circulatory phenomena were virtually the same as in the experiments in which the aorta of the splanchnic vessels had not been clamped. The respiratory changes occurred first. On making blood-counts, at the beginning of an experiment, it was found that in the cases in which the splanchnic circulation had been modified by clamping one or more of the supplying vessels, the number of red blood cells was strikingly diminished. This was in marked contrast with the comparatively slight changes occurring in the experiments in which such exclusion had not been made.

At the autopsy in this series of experiments no alterations were found in the abdominal viscera. There was no free fluid in the abdominal cavity. Usually the intestines were cyanotic. The stomach, when its blood supply had been excluded, remained normal, but it was noted in those cases that there was in the stomach and in the intestines a peculiar dark, bloody, gelatinous fluid which adhered closely to the mucous membrane. The walls of the hollow viscera were not thickened as in the other experiments. In comparison with the fore extremities, the hind were quite dry. The heart was pale, the pericardium containing some fluid. The heart stopped in diastole; the chambers were filled with diluted blood and there was considerable pressure in the aorta. In almost every instance the lungs were extremely edematous, much more so than in the experiments in which the splanchnic blood supply had not been excluded. Death in every instance was due to asphyxia, as in the first series.

*Effect of the Varying Height of the Saline Column:* A series of experiments was also made upon the effect of allowing the solution to flow from different heights. It was found that increasing the height of flow usually raised the blood-pressure. Great irregularity was noted in the change of the blood-pressure. In some instances there was but a slight rise, in others considerable. In the same experiment, at different times, the rise in the blood-pressure might not be equal to that produced by an elevation made earlier or later; that is to say, there was no direct ratio between the elevation and the rise in the blood-pressure, neither was there any ratio between the rise and the amount of saline the dog had received previous to the elevation of the bottle.

*Some Drug and Other Effects:* After a considerable amount of saline had been infused, the inhalation of chloroform, even in small dosage, produced a very marked depression on the circulation.

Upon the administration of strychnin or nitroglycerin, their usual physiologic actions were noted, though to a lesser degree.

Thermal, electrical and mechanical stimulation of the tissues produced the usual effects, *e. g.,* burning or crushing the paw caused a rise in the blood-pressure and an increased respiratory rhythm, manipulation of the larynx, a reflex inhibition of the respiration and the heart, etc.

*Effect of Varying Temperature, etc.:* No matter what the temperature, the effects were eventually about the same. When the solution was cold, the heart-beats were diminished and the strokes became longer. Frequently at the beginning there would be a fall in the blood-pressure, after which in many cases the usual rise observed in all saline infusions would occur. If the lost pressure was not regained during the flow, it was immediately on cessation of flow, with a return to the previous rapidity and length of strokes. Hot saline produced the opposite effect, *viz.,* an increase in the rapidity and a diminution of the length of the strokes, with a rise in the pressure. On cessation of the infusion the strokes would resume their former rate and length and the blood-pressure would fall to its previous level. The results were then almost ultimately alike. Even extreme variation in the temperatures of the solution produced but minor alterations in the temperature of the body. The effects of saline infusion were almost wholly mechanical and physical,—within a reasonable range they were independent of variation in the temperature, the rate of flow, the height above the animal, and the vein into which it was introduced. The mechanical factor consists in adding the force

of the infusion to the force of the venous blood-stream which raises the venous blood-pressure, thus increasing the output of the heart. The amount of the output has been proved to be dependent upon the venous blood-pressure.

One of the reasons why the infusion did not raise the pressure indefinitely was the escape of the solution from the circulation at a rate corresponding to the rate of the infusion. The escape occurred principally through the structures that normally absorb fluids—*viz.*, gastro-intestinal tract, to a much less extent through the mouth and respiratory tract, and still less into the tissues of the somatic area. The rate of escape of the saline solution through these channels almost equalled any rate of introduction we were able to devise. This was substantiated by numerous blood-counts, showing that after a certain dilution had been reached the count remained about the same. A secondary increase of blood-corpuscles was shown, although an enormous amount of saline was introduced during the observations, but in the experiments in which the splanchnic area had been previously excluded, by closing the splanchnic vessels, the dilution increased *pari passu* with the flow, strikingly diminishing the number of red blood-corpuscles. In these cases, the broncho-pulmonary tract eliminated larger quantities than it did in the experiments in which the "leaky" gastro-intestinal tract had not been excluded.

It might be supposed that in the experiments in which the great channel of elimination—*viz.*, the gastro-intestinal—had been excluded by closing the supplying vessels the blood-pressure would be raised higher than in the other experiments, but this was not observed. Neither was it found that the administration of an excessive amount of saline materially interfered with the response of the heart or the vasomotor mechanism to stimuli, as proved by the reflex inhibition from laryngeal manipulation, or crushing and burning the paws, by the administration of strychnin and nitroglycerin, as well as by the compensation that occurred on tilting the board.

*Conclusions:* The foregoing applies to the normal dog under surgical anesthesia. In experiments in which the blood-pressure had been lowered by a reasonable hemorrhage alone, saline infusion promptly restored the lost pressure. If the pressure had been lowered by the exhaustion of the vasomotor nervous system by afferent impulses set up by injury of the cerebro spinal or the sympathetic nervous system, the infusion would restore the pressure in proportion to the vasomotor exhaustion; that is to say, normal saline solution is effectual in shock in proportion to the

impairment of the vasomotor mechanism. If this mechanism has gone into resolution, infusion is without curative effect. If the impairment is considerable, the infusion will partially restore the pressure, etc. Taking into consideration all the facts, the reason why the blood-pressure is raised but little, if at all, higher than the normal is due to the rapid escape from the vessels and the action of the automatic mechanism in the medulla, which when the pressure rises above the normal diminishes the force and the frequency of the heart-beats and lessens the vaso-constriction in the area of peripheral resistance to reduce the pressure to the normal level. The peripheral resistance determines the height of the blood-pressure, no matter how swift the stream nor how great the volume of blood. The limitations of the effect of normal saline infusion must now be apparent. If the peripheral resistance is lost (break down of the vasomotor mechanism; that is to say, fatal "shock"), no amount of infusion can do more than temporarily or partially restore the blood-pressure, and death is inevitable. If the shock is much increased by regional accumulation of blood (so-called intravascular hemorrhage) as in operations on the splanchnic area infusion may be effective because the peripheral resistance is still present; that is to say, the vasomotor mechanism has not gone into resolution. If hemorrhage complicates shock and the vasomotor mechanism is still intact, infusion is effectual. Such proportions may be multiplied.

The foregoing deductions explain why injuries of the somatic area, such as mangling of limbs in railway accidents, are frequently but little, if at all, benefited by saline infusion. It is true that in almost every case an artificial pulse may be produced, even a pulse of considerable volume, but it is without resistance. It will disappear almost as quickly as it came, and no amount of infusion will sustain the circulation in such a case because the vasomotor mechanism has gone into resolution, destroying peripheral resistance, hence no blood-pressure can be created.

ILLUSTRATIVE CASE (Abstract): Brakeman, aged 25, in previous normal health, as proved at autopsy, was thrown under the trucks of a railway carriage, losing both legs above the knees. There was considerable hemorrhage.

Circulation: Pulse 152, small volume, rhythmic, slight tension. Nails, bluish; small superficial veins of chest and abdomen prominent; blood vessels of the lips and face distended and of venous color, giving a cyanotic pallor; pulsation in the neck marked, indicating toneless vessels; surface moist and cold, presenting bluish tinge.

*Respiration:* Rate 39; inspiratory phase, quickened and shortened; expiratory phase, relatively lengthened; pause increased; extraordinary muscles in light action; slight rhythmic movement of the larynx and *alae nasae.*

*Nervous System:* Mind clear and alert; special senses acute; complains but little of pain; is restless and begs for water.

*Discussion of the Physiologic State:* The massive mechanical irritation and exposure of the nerve endings and nerve trunks produced an excessive action of the vasomotor and cardiac centers, especially the first, leading the exhaustion. Proportionately to the degree of exhaustion the "peripheral resistance" is diminished. Proportionately to the diminution of peripheral resistance the general blood-pressure is lowered and the venous return diminished. Proportionately to the diminution of the venous return the output of the heart is diminished, and proportionately to the diminished output of the heart the volume of the pulse and the general blood-pressure is diminished. This "toneless" state of the vascular system, then, is due to the loss of the "peripheral resistance," which in turn is due to the exhaustion of the vasomotor mechanism, which is due to the excessive stimulation, owing to massive mechanical irritation of the nerve supply of the lower extremities, by the wheel of a car. In this toneless state the larger arterial trunks are relatively empty, so that the blood thrown into the arterial trunks with each contraction of the heart produced a high but short wave, accounting for the marked pulsation in the arteries of the neck; the wave then, when it reaches the extremities (*e. g.,* radial pulse) is proportionately diminished or lost, is abrupt in ascent, is not sustained, and has proportionately lost its resistance. The capillary circulation is correspondingly diminished, producing the pallor which, together with the loss of heat by perspiration, produces the cooling of skin. The diminution of the capillary pressure proportionately lessens the venous flow, thereby causing an accumulation of blood upon the venous side, which accounts for the prominence of the small superficial veins and the bluish tinge of the skin—"cyanotic pallor." The acceleration of the blood-pressure is reduced, the heart-beat is increased in frequency and in force; and, other things being equal, when its intake is diminished it beats with increased force and frequency. (There are many important questions that this discussion has opened, but as they are not pertinent to our present inquiry they will not be discussed.)

The respiration is increased in frequency in accordance with a well known law governing its automatic center—*viz.,* the dimin-

ution of oxygen in the blood causes an increased respiratory action, and when the blood reaches a certain degree of cyanosis the extraordinary muscles of respiration are brought into action whether obstruction is or is not present. There being no obstruction present, and the extraordinary muscles having no resistance to overcome, their work is so light as to give but little evidence of their action—the inauguration of their action being rather an indication of the degree of cyanosis, which in turn indicates the degree of circulatory failure. The amount of blood under these conditions actually circulating through the lungs is proportionately diminished, which would be in effect a hemorrhage, an intravascular hemorrhage. The effect upon the respiratory mechanism is essentially the same as in an actual external hemorrhage. Owing to the diminished nutrition and excessive action the respiratory mechanism becomes fatigued, the earlier indications being an increased pause and a quickened inspiratory phase. During 20 minutes, 2,000 cubic centimetres of normal saline solution at 100° F. was infused into the median basilic vein (other features of the case will not be discussed). The pulse was reduced in frequency to 124. The volume was fully as large as normal, the ascent of the wave was abrupt, the fall equally so. The tension remained low. The patient perspired freely and was less restless. Cyanosis diminished. Superficial veins remained about the same. Pulsations of the neck were more marked than before. The patient was not so restless. There was an improvement in most of the symptoms, but what of the vasomotor mechanism? The ascent and descent of the wave was as sharp as before. There was an enormous increase in the volume, but only slight in tension. The arterial trunks in the neck oscillated even more than before. The superficial veins were even still more prominent. The skin continued to have a cyanotic pallor.

These several phenomena show that the vasomotor impairment and impending break-down still existed. Though a large pulse was artificially created, the patient's chances for recovery were virtually what they were before. The effects of the saline solution gradually passed away, and an hour later another saline infusion of 1,500 c.c. was given. This time the effect was not so marked and were less sustained than in the preceding. All of the symptoms rapidly grew worse and the patient died at the end of four hours. After the first infusion had been given oxygen was administered. During the administration respirations were diminished in frequency and the cyanosis was lessened. The participation of the extraordinary muscles of respiration was diminished.

This discussion has been extended for the purpose of defining a well-marked and fairly characteristic group in which saline infusion is of but temporary aid and in which it does not alter the essential conditions present. The vasomotor break-down is an impairment that cannot be relieved by saline infusion. Drugs are equally ineffective in these cases for the same reason that, although the heart may be stimulated, there being no peripheral resistance, no blood-pressure (pulse) can be created, and death is inevitable. Drugs having action upon the vasomotor mechanism are equally powerless, because this mechanism having become exhausted, it cannot respond. This also gives a clear reason for the benefits of infusion in cases of hemorrhage alone or hemorrhage with shock, by restoring the normal volume of fluid and adding force to the venous stream.

In shock (vasomotor impairment—*i. e.,* lowered peripheral resistance) the benefit is due to the force added to the venous circulation. The venous pressure falls *pari passu* with the diminution of the peripheral resistance (vasomotor impairment shock), so that the saline infusion supplies to the venous blood-pressure force which the decreasing peripheral resistance does not ordinarily supply. It must be borne in mind that the output of the heart is wholly dependent upon the venous pressure; that is to say, the infusion may merely tide over a circulatory crisis, during which other means for restoring the circulatory equilibrium and tone must be employed. In cases of dangeous hemorrhage the combination of oxygen inhalation with infusion is beneficial, because the reduction in the number of corpuscles so diminishes the amount of oxygen carried that it should be supplied in concentrated form, which, by virtue of the law of diffusion of gases, increases the volume's percent of oxygen in the blood.

### COCAIN AND EUCAIN

#### SUMMARY OF EIGHTY-NINE EXPERIMENTS

*Histologic Examination of Cords:* In the recovery experiments in the cases in which the solution was injected into the cord very great difficulty was experienced in locating the point of injection. Only in those cords in which no asceptic or antiseptic precautions had been taken at the time of injection could the track of the needle be traced with the unaided eye. Careful inspection of the cords in which aseptic precautions had been taken failed to reveal the point of injection. The cords were hardened and sectioned throughout the approximate area of injection. In but few instances was there any degeneration, infiltration, or hem-

orrhage found. In the non-aseptic cords the track of the needle
was readily traced by the slight congestion present. Sections
through this area after the cords were hardened showed some
small celled infiltration with some degeneration, and in one
instance a hemorrhage into the right anterior cornu. The
needle had traversed the right half of the cord to within one m.m.
of the anterior surface in this case.

*Effect Upon Peripheral Nerve Trunks:* The injection of
eucain or cocain into a nerve trunk so as to place all its structures
in contact with the drug produces an effectual physiologic "block."
By the word "block" is meant such condition of the nerve that
neither afferent nor efferent impulses can pass, the conductivity
being as completely interrupted as if the nerve were divided.
While general anesthesia prevents the appreciation of pain and
the production of voluntary motion, it does not prevent such other
afferent impulses as those caused by mechanical, thermal, or elec-
trical stimulation of the nerve endings or trunks, which produce
changes in the frequency and the amplitude of the respirations,
in the frequency and force of the heart-beats, and in vasomotor
action. Either eucain or cocain injected into a nerve trunk as
above described prevents the passing of such afferent impulses,
thereby preventing effects upon the respiration, the heart, or the
vasomotor mechanism—*i. e.,* shock. Under general anesthesia.
if the paw of an animal is subjected to the flame of a Bunsen
burner, after the lapse of a short time the leg is drawn up by the
contraction of groups of muscles in a deliberate but rather forcible
manner, removing the foot from the flame. General anesthesia,
no matter how deep nor what anesthetic employed, does not pre-
vent such action of the muscles. It seems, if the expression may
be allowed, to be an "unconscious purposive" action. Either
eucain or cocain injected into the path of these afferent impulses
prevents this phenomenon. If it is intended to produce an imme-
diate effect it is necessary to make a thorough injection. If a
little time is allowed to elapse, the solution need not be directly
injected into all the parts of the nerve-trunk. Even if injected
underneath the sheath, without penetrating the substance of the
nerve-trunk, a "physiologic" block may be produced. No unfav-
orable later effects were noted. In a number of cases in which
the nerves were thus blocked, and the animal allowed to recover,
there was but temporary functional impairment, and in no instance
was there evidence of neuritis or of degeneration following. The
effect of the eucain and cocain upon nerve structures is apparently
the same as their well-known general effects upon the protoplasm;

that is, they temporarily suspend its functional activity. They form no chemical combination and cause no destruction either of its physiologic properties or of its substance. As to afferent impulses, it was found that the cortical discharges of the brain were blocked, either when they originated as a voluntary action, or when they originated as an artificial convulsion produced by the administration of the essential oil of absinthe. Even powerful electrical currents applied to the nerve trunk, near the block, were found to be incapable of forcing their impulses through the "block." That which has been said of the effect of cocain thus applied to the nerve trunks may be said of like injections into the spinal cord. The effect upon the optic nerve is that of blocking the impulses of the light waves through this nerve, at least partially, and were the injections given directly into this nerve the "block" would probably be complete. Either eucain or cocain when applied upon the medulla or fourth ventricle within a few seconds suspends the action of the respiratory center. This suspension is characterized by a gradually increasing slowness of respiration, together with gradually decreasing amplitude, so that within 30 seconds respirations cease. The blood-pressure, in nearly every instance, suffers a profound depression, the nature of which is a gradual decline such as is observed on making a cross section of the cervical spinal cord; that is to say, the vasomotor center or paths are anesthetized.

Another effect of the application of eucain or cocain upon the medulla or the floor of the fourth ventricle is immediate complete general anesthesia and immediate total loss of all voluntary action. The corneal reflexes are at once abolished and the pupils are dilated. When the paws of the dog are exposed to the flame of a Bunsen flame the legs are not drawn up, the blood-pressure is not altered, and the heart's action is not affected. It is needless to say that there are no respiratory changes. In other words, application of these anesthetics upon the medulla or the floor of the fourth ventricle suspends temporarily all the manifest functions of that organ excepting the heart's action, and that is modified. General anesthesia may be indefinitely prolonged by repeated applications. Upon the vagi the effect of an injection of these drugs is to suspend their inhibitory action. The action of cocain is probably a little more prompt than that of eucain, the latter, however, seemed to be quite as effective as the former. Cocain and eucain block the impulses set up by electrical stimulation in nerve-trunks even after death; that is, if after the death of an animal a nerve-trunk is stimulated, within a certain time the

muscles supplied will be thrown into contraction; but if cocain
or eucain is injected into the nerve-trunk and a stimulus applied
above it, no contraction will occur.

The physiologic action of cocain and eucain, both local and
general, are so nearly alike that one description may serve for
both. The first effect, observed after the intravenous injection,
is a temporary increase in the blood-pressure. This increase
appears almost immediately, and continues for a brief period of
from five to 20 seconds, when the blood-pressure returns to or
near its former level. The heart-strokes forming the curve are
usually a little shorter, and the rapidity of the heart's action some-
what increased. No definite vasomotor change was indicated by
the peripheral venous or peripheral arterial manometers. A water
manometer recording the splanchnic blood-pressure indicated a
rise out of proportion to the rise in the general blood-pressure.
In rare instances there was a fall in the blood-pressure, but com-
pensation was immediately inaugurated and the lost pressure was
quickly regained. In overwhelming doses with lethal effect the
general blood-pressure, in fact all the pressures, rapidly sinking to
the abscissa line. It was noted that when the animal was under
the systematic effect of these drugs the blood-pressure curve was,
as a rule, not so regular as under normal conditions. It was also
noted that in a number of experiments the length of the stroke
of the writing style, expressing the heart's action, was shortened
under the systematic effects of these drugs. This irregularity of
the blood-pressure curve was similar to the irregular curve when
the animal was under physiologic dosage of atropin or when both
vagi had previously been severed. It was also found that when
animals were under the effect of these drugs, stimulation, by
applying the electrodes upon the vagi, did not produce normal
characteristic effect; that is to say, that while in normal condi-
tions the application of a Dubois-Reymond electrode upon the
vagi causes slowing or arrest of the heart, in animals under the
systematic influence of cocain or eucain the application of such
stimulation to the vagi in most instances produced little or no
effect. In a number of experiments it was observed that if, after
having secured a control tracing of the inhibitory effect of intra-
laryngeal manipulation, the animal was subjected to a physiologic
dosage of cocain or eucain, a like manipulation of the larynx
usually produced no inhibition. In the experiments in which
inhibition was noted it was in most instances less than normal.
The same may be said of other experiments upon the superior
laryngeal nerve. The physiologic effect of cocain and eucain in

this respect is quite analogous to that of atropin, though the effect is not so marked. The increase in the blood-pressure after the administration of cocain is in a measure similar to that which follows section of both vagi. Taking into consideration all of the evidence, it would seem that cocain and eucain partially or wholly suspend the inhibitory function of the vagi, whether produced by direct or indirect stimulation. While not prepared to make a positive statement on the subject, it appears that the increased rapidity of the heart's action under the influence of these drugs was due to the removal of the vagal influence and not to stimulation of the accelerators. The splanchnic area, especially the veins, when the abdominal viscera were subjected to exposure or irritation, or both, was dilated, the intestines became red, extremely congested, and often livid. When the animal had been given a physiologic dose of cocain or eucain and exposed to like experiment the splanchnic vessels did not dilate, excepting those at the bases of the intestines. The arteries became decidedly smaller and the intestines a peculiar palish red. In a large series of control experiments it was found that, with but rare exceptions, such irritation or exposure of the splanchnic area caused a fall in the general blood-pressure proportional to the exposure or irritation and the condition of the animal. In some instances the fall was extremely rapid and the animal soon died, but in a series of experiments in which cocain was systematically administered there was but a slight, if any, fall in the general blood-pressure. There was a striking difference between the results in the control experiments and the "cocain" ones. In order to make the comparisons more reliable double experiments were performed. Two animals of as nearly the same size and under as nearly the same conditions as possible were placed side by side on similar dog-boards, and precisely the same experiments were performed simultaneously upon each. In every instance the benefit of any doubt was allowed to control the dog. The writing style recording the blood-pressure and the respiratory action of each was placed in a vertical line, so that direct comparisons could be accurately made. The result of these double experiments may be summarized as follows: In the control dogs exposure and manipulation of the intestines produced a fall in the blood-pressure; in the cocain and eucain dogs, as a rule, no fall occurred. The cocain and eucain dogs endured more mechanical injury than the control dog. The latter in every experiment died first. In burning the hind feet in the animals the blood-pressure in the control rose higher and more promptly than in the cocain and eucain dogs.

In crushing the testicle the blood-pressure fell more promptly and a greater distance than in the cocain or eucain dogs. The same may be said of the manipulation of the larynx, stimulation of the vagi, operations in the pharynx—in short, of every portion of the body. The comparison between the appearance of the abdominal viscera in the control dog and that in the cocain or eucain dog is that in the latter the intestines were of a peculiar shade of pale red, and the vessels were, if any change was noted, of less calibre than before the experiment; while in the control dog the vessels were all engorged, the viscera exceedingly red, and in many instances livid. It was at once apparent that the difference between the blood in the splanchnic area in these two animals was very great. Even the inferior vena cava was smaller in the cocain animals. The effect upon the circulatory apparatus, first, an immediate rise in the blood-pressure lasting a few minutes, followed by a compensatory fall. Later, a gradual rise occurs. The inhibitory influence of the vagus is partially or wholly suspended. The vasomotor reflexes are considerably lessened. The circulatory apparatus is less responsive to stimulation. The latent period of vasomotor reflex action is markedly increased. The vessels of the splanchnic area are contracted.

There is but little doubt that there is an increased tendency to clotting. Upon the respirations a small dose seemed to act as a stimulant. A medium dose seemed to lessen the length of the respiratory stroke, while a large dose caused respiration to gradually diminish. It was frequently observed that if a series of injections of these drugs were administered at given intervals a very marked tolerance was acquired, so that finally but little effect could be produced. It was also observed that animals under the influence of these drugs were more difficult to maintain in the condition of even surgical anesthesia. More general anesthesia seemed to be required, and the animals had a tendency to come unexpectedly out from its influence.

### SPINAL CORD ANESTHESIA

*Injection into the Cord:* In 1897, after performing the experiments upon nerve-trunks showing that cocain was capable of producing physiologic section, that is to say, the afferent or efferent impulses could not pass the point cocainized,—and after having performed amputations on the human subject without pain and without shock by this method, similar procedures upon the spinal cord were suggested. The experiments along this line consisted in injecting the solution directly into the substance of the cord. This produced immediate anesthesia at all the points

with which the cocain came in contact. Although the anesthesia was immediate and complete, and for operative purposes was entirely satisfactory, it was obvious that this procedure necessitated a physical damage to the cord.

Recovery experiments were made as follows: The cord was anesthetized by injecting cocain directly into its substance by means of a fine needle. The completeness of the anesthesia was proved, the animal allowed to recover, and after the lapse of varying periods of time was killed. The cord was subjected to microscopic examination. While in some of the cases it was impossible to detect any microscopic damage to the cord, there was found some round celled infiltration and disturbance of the histologic arrangement. It was at that time concluded that this was not a justifiable procedure in any but most exceptional cases. Later experiments were made by injecting cocain into the subarachnoid space. In dogs this space is so small that it is necessary to expose the cord in order to make an injection without traversing the cord. The injection of a 1% solution of cocain into this space produced almost immediate anesthesia.

*Subarachnoid Injection: Effect on the Circulation.* The effect of injecting a solution of cocain into the subarachnoid space in the lumbar region was an immediate fall in the blood-pressure, the beginning of the fall being almost coincident with the contact of the solution of cocain with the cord. The depth of the fall was proportional to the completeness and the anatomical parts involved. The curve in the descent of the blood-pressure was gradual and even after which a regular line was maintained for some distance, which indicated the loss of vasomotor control. The effect upon the blood-pressure when the medulla or the fourth ventricle was cocainized was the greatest of all, the pressure falling almost to the abscissa line. When all the cord had been subjected to the influence of cocain and the pressure had fallen as above described, if any part of the body below the level cocainized was subjected to burning, crushing, or any other mechanical, thermal, or electrical stimulation, no rise in the blood-pressure occurred. There was usually but a trifling amount, if any, of compensation after the fall of the blood-pressure until the cocain effects had passed off.

*Effects on Respiration.* The immediate effects on respiration, of a subarachnoid injection of a comparatively small amount of cocain in any part of the spinal cord, not involving the medulla, is acceleration. The application of a 1% solution of cocain upon the medulla or the floor of the fourth ventricle produced

within a period of time ranging from a few seconds to a few minutes, complete respiratory paralysis. There is first loss of the intercostal and extraordinary muscles, then the abdominal muscles and lastly the diaphragm. The action of the diaphragm becomes shallower at each contraction until it is entirely paralyzed.

The membranes of the cord are so nearly inelastic that for the present purpose they may be regarded as being so, while the cord itself is so nearly incompressible that it may be considered so. The subarachnoid space is always filled with its own fluid. If additional fluid is added, it must cause a displacement similar to that of fluid in a capillary glass tube. The rapid and uncontrollable ascent of the anesthesia of the cord was most striking. In order to better study this a series of injections was made with cocain solution colored with methylen blue. It was found that an ordinary injection of the lumbar region of one-half dram of this solution stained the entire cord and the under surface of the brain within 30 seconds. All the various localized functions of the cord and medulla were with rapidity anesthetized. The respiratory center in the medulla, for example, could be anesthetized by lumbar subarachnoid injection within a few seconds, so rapidly did the fluid pass up the cord. Marked fall in the blood-pressure and cessation of the respiration occurred within a few seconds, after a rather forcible injection in the lumbar subarachnoid space. The fluid ascended about as readily in the vertical posture as in a horizontal. There can be but little doubt that the effect is due to the local contact of the nerve structure and not to absorption. This view is in full accord with the action of cocain on other nerve tissue. A solution injected with considerable force into the lumbar subarachnoid space was attended immediately by convulsions. The convulsions were due to the stimulation of the convulsive center in the medulla. The dosage used in these experiments was purposely made large to determine the control, or rather the want of control, the operator could have upon the extent of the anesthesia. In control experiments in which normal saline solution was injected into the spinal cord an immediate fall in the blood-pressure occurred, but compensation quickly followed. The respirations were but slightly affected. There was the most striking difference between the overwhelming paralysis in the one case and the want of it in the other. The experiments showed that the operator has but little control over the extent of the anesthesia produced under the subarachnoid injection. While direct injection into the cord gave a complete control of the extent, it produced a distinct mechanical lesion. In the

clinical reports of the subarachnoid anesthesia the experimental data have been corroborated. This was most strikingly exhibited in a case described by Fowler in which the anesthesia during three minutes extended up to the level of the clavicle, at which time the patient became cyanotic and artificial respiration was necessary. Other observers have noted the marked effect on respiration, the lowered blood-pressure, and the rapid pulse, the latter indicating that the cocain solution was affecting the centers of the medulla. In 692 cases there were six deaths that were attributable to the anesthesia, a mortality rate at least fifty times greater than that of chloroform.

### ON THE CLINICAL APPLICATION OF THE EXPERIMENTAL EVIDENCE

*Operations on the Extremities: Leg.* The "blocking" method was employed independently by Dr Rudolph Matas, of New Orleans, of which his brilliant monogram on anesthesia gives a full account. Applying the so-called physiologic "blocking" properties of cocain or eucain to surgical practice, we have been enabled to perform certain operations upon the extremities without causing pain and without shock by injecting a 1% solution of cocain into the supplying nerve-trunks. The external cutaneous nerve is so superficial that it is readily accessible. The anterior crural is readily exposed in its relations with the artery and the sciatic at the margin of the gluteal fold along the inner border of the biceps muscle. In operations performed upon the area supplied by the "blocked" nerve-trunks the afferent impulses cannot reach the central nervous system. There is, therefore, neither pain or shock. This method is of the greatest possible importance in operations in which general anesthesia is for one reason contraindicated. The operations under these circumstances cannot cause any more shock than if the member had no connection with the body, as the "block" for all such purposes is equal to a physiologic amputation.

In this manner I have five times performed amputation of the leg below the knee, and in all but one the patient was not aware that the operation was performed until told of it afterwards. It is necessary to control the patient well. After preliminary preparations have been made, the patient's attention should be diverted. I have usually said that an examination and a dressing would be made requiring considerable time and that the operation would be performed next day. In the meantime the eyes were covered. In the one case the patient became aware of the progress of the operation by hearing the noise of the saw while divid-

ing the bone. The "block" continues from 25 to 30 minutes. The clinical observations are in entire accord with the experimental evidence.

*Operations in the Area of the Distribution of the Ulnar Nerve: Remarks.* The superficial position of this nerve at the elbow joint enables the surgeon to apply a cocain or a eucain "block" almost painlessly by inserting a hypodermic needle, first into its close vicinity, then into the trunk itself, injecting the solution on its way. After the lapse of ten minutes the entire area supplied will be rendered anesthetized, and if the patient's attention is diverted operative procedures, such as amputations, resections, may be performed painlessly and without the patient's knowledge.

<div align="center">REPORT OF CASES</div>

CASE 1: A railway employee whose hand and little finger were severely crushed within the area of the distribution of the ulnar nerve required amputation and revision. Bending the elbow, a wheal was produced by injecting a 1/12% solution of beta eucain, thereby creating a painless path to the nerve-trunk which was then anesthetized. In a few seconds there was complete anesthesia, and the finger and the corresponding metacarpal bones were removed while the patient was an interested spectator. The night following this operation the patient complained of a burning sensation over the distribution of this nerve. There was some local tenderness at the point of injection, but this disappeared after several days.

CASE 2: A small boy discharged a pistol, which took effect in the ulnar side of the hand, tearing away the soft parts and a portion of the fifth metacarpal bone. By "blocking" the ulnar nerve at the elbow the wound was revised, and the fragments of the bone removed without pain. In this case there was no complaint of the burning sensation described in the preceding. The wound healed readily.

CASE 3: In a tubercular patient a local focus appeared in the metacarpo-phalangeal joint. In performing an operation for the removal of this focus, the ulner nerve was "blocked." At first an attempt was made to secure anesthesia by injecting the solution around the nerve, but after waiting five minutes it was found that anesthesia was only partial and that it was necessary to inject the nerve itself. In performing the operation it is best to fix the nerve well against the bone and insert the needle gradually, as anesthesia occurs in advance of the needle. After such

an injection the anesthesia was complete and the operation was performed painlessly. The patient complained of some burning the first night, but the second day it decreased and was not again experienced.

*Observations:* In two other cases this nerve was in a similar manner "blocked." In each the anesthesia was complete in five to 10 minutes and no after effects were noted. In no case was there any interference with the function of this nerve in consequence of this injection. Neither did the points at which the injection was made remain tender. No neuritis followed.

*Amputations at the Shoulder Joint:* Amputations at the shoulder joint are usually indicated on account of a serious accident or disease, and in consequence such operations are frequently performed under unfavorable circumstances. There has been a considerable mortality following this operation, even under the more favored conditions. In operations for malignant disease in the aged, and in operations in the presence of profound depression or shock, general anesthesia adds seriously to the danger. There are many instances of contraindication to the use of general anesthesia. A method by which this operation may be performed without general anesthesia, without shock and without hemorrhage, was devised in accordance with the experimental evidence set forth in the preceding pages, and put into practice in June, 1898.

*Technique:* The technique is based upon the fact that nerve-trunks may be safely and effectually subjected to a physiologic "block" by injecting cocain or eucain in a comparative weak solution, and that arteries may be, with entire safety, temporarily closed without injuring their walls. Fortunately in the application of these principles, in amputation of the shoulder joint the subclavian artery is in close surgical relation with the brachial plexus so that the same incision may be utilized for exposing the nerve and the blood supply.

### REPORT OF CASES

CASE 1: Female, aged 74, was suffering from sarcoma of the arm, situated in the lower third and extending well down to the elbow. There was a metastatic growth in the axilla. She was suffering great pain and the tumor was growing rapidly. Owing to her extreme age, an amputation at the shoulder joint by the methods hitherto in vogue, giving a general anesthesia without "blocking" the nerve-trunks to protect her against the afferent impulses caused by the mechanical irritation of the amputation,

thereby producing shock, would have been a risk too great to
assume. It was decided to perform the operation by employing
the technique above described. An incision was made along the
outer border of the sternomastoid muscle under 1/10% infil-
tration cocain anesthesia. The incision was carried through the
superficial and the deep fascia, exposing in the first part of the
incision the external jugular vein. The lower part of the incision
was carried well down on the clavicle. The omohyoid muscle was
retracted downward, the anterior angle of the trapezius backward
and the posterior margin of the scalenus anticus forward, thereby
exposing the trunks of the brachial plexus, and by extending the
dissection a trifle farther downward and inward the arching sub-
clavian artery was brought into the field. In making this dissec-
tion it is important to keep the field of the operation entirely free
from blood, so that the translucency of the tissue will permit the
ready recognition of the anatomical structures in their minutest
detail. It will then be possible to detect small nerve twigs before
they are encountered and enable the operator to subject them to
local anesthesia in advance. In this way the area supplied by
these branches may be rendered anesthetized. The small vessels
may be caught with narrow bladed forceps between which the
incision may be carried. The smaller nerve twigs are usually
found running along the blood vessels or in the connective tissue
planes. It was observed in this dissection that in the deeper struc-
tures the sensory nerve supply is not so abundant as in the more
superficial. After exposing the trunks of the brachial plexus,
there being but a slight amount of pain in the dissection, they
were subjected to a physiologic blacking by injecting first on
their outer covering, then into the substance, a ½% solution of
cocain, just sufficient to cause a localized swelling. It required
but a small amount of solution to accomplish this. After injecting
each trunk there was a total loss of sensation and of motion in
all the parts supplied by the brachial plexus. The subclavian
artery was then closed by means of a special clamp, over the
blades of which rubber tubing was drawn. The blades were then
approximated by adjusting the screw sufficiently to close the
lumen of the vessel. The patient was then told that the operation
would not be performed at that time, but would be deferred until
the next day. A towel was thrown over her eyes, and under the
pretext of making a careful examination of her arm the amputa-
tion was made without her knowledge. The flap on the outer
and posterior aspects over the deltoid was made rather low,
because of the subcutaneous distribution of the branches of nerves

from the cervical plexus, which of course had not been included in the physiologic block. She experienced no pain except a slight one as the incision was carried around the posterior surface of the upper portion of the arm supplied by the supra-acromial nerve. The pain was, however, comparatively slight, and was felt only during the incision of the skin. During the disarticulation the patient was not aware that she was being touched. After the operation had been completed it was found that there was absolutely no shock and that the operation had made no appreciable impression on her. The vessels were all picked up and tied before releasing the clamp from the subclavian. The total amount of cocain used in the operation was about one-eighth of a grain. A portion of this amount was recovered by sponging away the free solution in the wound. When the patient was returned to her bed the patient was not aware that her arm had been removed. She soon missed it and manifesting some excitement was informed by the nurse. She experienced some pain a few hours after the operation and vomited several times the first night. She made a good recovery from the operation and there was nothing in the after-progress of the case different from operations performed in the usual way.

CASE 2: Amputation of the arm at the middle was performed by the same technique as the preceding without producing any pain and without the slightest shock. Patient made a good recovery. The operation was performed on account of. moist gangrene of the forearm in a patient having advanced pulmonary tuberculosis.

*Amputation of Half the Shoulder Girdle: Remarks.* This operation has been performed a number of times by various methods. The purpose of discussing it is to point out a technique by means of which hemorrhage and shock may be wholly avoided. Under general anesthesia an incision is made over the clavicle and the inner half of this bone is resected, after which the subclavian vein and the trunks of the brachial plexus are exposed. The trunks are then subjected to a physiologic block of cocain and eucain in comparatively weak solution—say ½%. The brachial plexus is next severed and the artery and vein closed by ligature. The incision for the further technique in removing the scapula will vary with the object for which the operation is done. The amount of shock will be limited to what will be produced by making the incision through the structures supplied by the nerves from the cervical plexus, which is almost nil.

*Observation of the Pharynx:*  Clinical experience, as well as physiologic experiments, have demonstrated that when the pharynx is subjected to a considerable manipulation, especially that portion nearest the glottis, reflex inhibition both of the respiration and of the heart may occur.  The respiratory inhibition is the more frequently produced.  In the cases in which manipulation required considerable force the heart may be inhibited, causing collapse.  I have observed this reflex inhibition of both the heart and the respiration in removing a tumor of considerable size from the nasopharynx.  In operations for removing adenoid growths from the nasopharynx these phenomena have also been observed. In extracting large foreign bodies collapse may be produced.  Not infrequently, in performing difficult operations in this portion of the pharynx, reflex inhibition confuses the operator.  The respiratory inhibition is likely to give the impression that the patient is suffering from mechanical obstruction.  The inclination might be to clear out the upper respiratory passage, but this additional irritation would increase the symptoms.  In the experiments it was found that reflex inhibition in this area may be prevented by the local application of a 2% solution of cocain.  The solution may be as weak as 1%, or even ½%, and be effectual  A hypodermic injection of atropin prevents reflex inhibition of the heart. In cases necessitating the removal of adenoid growths and tumors of the pharynx the efficiency of these drugs was proved.  It is advisable, before beginning the technique of an operation involving this area, to make a local application of a solution of eucain or cocain, and a hypodermic injection of atropin, to prevent reflex inhibition.  If during an operation inhibition does occur, the distinction between inhibition and obstruction must be borne in mind, for if the case is one of obstruction there will be increased respiratory efforts, but if it is a reflex inhibition respirations instantly cease.   In obstructions the pulse continues unaltered for some time before it becomes markedly slower.  In reflex inhibition the pulse is instantly and markedly slowed or arrested.

*Laryngotomy:  Remarks.*  Not infrequently in this operation at the moment the larynx is opened the patient goes into a state of collapse from which he may never recover.  This operation is more frequently performed on children, oftentimes in great haste, under the stress of circumstances.  If the operation is performed through the cricoid, collapse at the moment of entering does not occur.  If made higher, it is very likely to occur, the reason being that in the higher operations the inhibition area of the larynx is mechanically stimulated.  This causes a reflex

inhibition, as in operations upon the pharynx. The superior laryngeal nerves are endowed with very strong inhibitory functions, which are more active in the upper part of the larynx. The clinical observations are in entire accord with the experimental evidence.

### REPORT OF CASES

CASE 1: Dr M. called in a colleague to aid in performing a laryngotomy upon a child who had a grain of corn in the larynx. The operation was successful until the larynx was opened, when suddenly collapse occurred, resuscitation seemed impossible. During the first stages of the collapse the corn was removed. Artificial respiration was maintained for a time, though life seemed extinct, when suddenly respirations began and there was an uneventful recovery.

CASE 2: I was called to see a child three years old having a large bean lodged in the larynx. The history of the case was that while the child was playing with the bean, in a fit of laughter, inspired it into the larynx. Paroxysms of coughing followed. These occurred at intervals. Each time the child stopped breathing, became cyanotic and apparently dead. After a brief interval respirations returned, another paroxysm soon followed with a repetition of the collapse. From these symptoms alone the location of the bean was diagnosed as being in the upper part of the larynx. An operation under local anesthesia was performed. The incision was made through the cricoid cartilage, below the so-called inhibition area, and the laryngeal mucosa was treated with a 2% solution of cocain, after which the larynx could be readily explored, the bean located and removed without inducing reflex inhibition.

*Observations:* Cases might be multiplied, but the foregoing are typical. The difference between reflex inhibition and obstruction is very marked. Reflex inhibition cannot be produced by a foreign body at any point below the so-called inhibition area of the larynx. The importance of the use of local anesthesia, to prevent reflex inhibition in laryngeal operations, cannot be overstated.

In all the operations upon the larynx, especially in laryngectomy and intralaryngeal procedures, the use of cocain and eucain is of the greatest importance. In laryngectomy especial attention has been called to the collapse that not infrequently appears while removing the larynx from its attachments.

Bardenhauer encountered this three times in one case while

inflating the Trendelenburg apparatus. In intubation sudden
death frequently occurs, the collapse being due to reflex inhibition
of either the respiration or the heart, or both. Cocain or eucain
applied on the mucous membrane wholly prevents such reflex
inhibition. If such local application cannot be applied, all the
necessary arrangements for the maintenance of the artificial res-
piration may be made in advance. A hypodermic injection of
atropin will prevent the cardiac inhibition, so that, without the use
of local anesthesia, atropin, with artificial respiration, may be
depended upon to carry the patient over the inhibition crisis. In
one hundred and fifty-six intubations I have encountered reflex
inhibition six times, twice fatal, and they occurred before the
nature of the inhibition was comprehended. Since making use of ·
the experimental data, no case has been lost from reflex inhibition
or "laryngeal collapse."

Death cannot occur as a result of reflex inhibition if a pre-
liminary hypodermic of a physiologic dose of atropin is given.
The use of cocain is not practical in intubations for diphtheritic
stenosis.

*Clinical Summary:* In the clinical use of cocain and eucain
particular attention is called to a most important feature—*viz.*,
that shock is almost wholly avoided as all afferent impulses are
blocked. It is now known that afferent impulses set up by injury
or operation are the causes of shock. These impulses are but
slightly modified by general anesthesia. The afferent impulse,
constituting pain, is abolished by general anesthesia, but those
affecting the vasomotor, the respiratory, and the cardiac mechan-
isms are not controlled; but cocain or eucain absolutely blocks
their passage, making a physiologic amputation of the part. These
anesthetics wholly prevent reflex inhibition, the principal causes
of collapse in operations and injuries—*e. g.,* operations on the
larynx and pharynx. Given hypodermically, the experimental
evidence shows that they diminish shock in operations on the
splanchnic area and absolutely alter this area in the processes of
operation or exposure, as abundantly proved by the series of
double experiments.

I have had but two opportunities of testing this clinically,
both in operations for gun-shot wounds of the intestines, and in
each the experimental evidence seemed to be corroborated. Com-
parative results require such a large number of observations that
I prefer for the present to offer no more than the clinical
suggestion.

ON THE EFFECT OF TEMPORARY CLOSURE OF THE CAROTID ARTERIES
SUMMARY OF NINETEEN EXPERIMENTS

*Histologic:* The gross specimens presented an oval outline on section at the constricted portion. This flattening of the artery was more marked in those carotids which had been clamped for some hours and in those in which the clamps had been tightly adjusted. The histologic appearance of arteries clamped for short periods and examined at once showed but slight change. Arteries clamped for periods of from 15 minutes to half hour showed little effect other than a slight tearing of endothelium at the extremities of the oval. Those clamped for an hour showed a greater amount of distortion of the endothelium at the margins of the oval with some separation and endothelial cells, which were massed between folds of fenestrated membrane. The elastic layers were slightly distorted at the constricted portion. The elements of the middle layer were massed at the extremities and somewhat disarranged. The adventitia was unchanged. The histologic appearance of the carotids from the recovery experiments varied with several conditions. The amount of pressure exerted by the clamp, the presence or absence of wound infection, and the length of time the clamps were allowed to remain on the artery, modified the results.

Some specimens clamped too tightly for four or six hours showed marked degeneration of the middle coats with edema and a thickening and disarrangement of the intima, with loss of endothelium and a very perceptible narrowing of the lumen; others were thrombosed, some were necrotic; but in those carotids in which care was taken to so adjust the clamps as to exert only sufficient pressure on the artery to close its lumen, the histologic changes were unimportant. A clamp adjusted too tightly caused pressure necrosis in a few hours, while other carotids were clamped for from 24 to 48 hours without notable damage to the arterial walls. The intima and elastic membrane were but slightly affected though the media showed some evidence of degeneration. The adventitia was but slightly altered.

The presence or absence of infection of the wound was of great importance. In those cases in which an infection appeared the arteries showed the greatest changes. In many instances the artery was necrotic at the clamped portion, and in some instances it was severed. The media and adventitia, both above and below the constricted portion, showed round celled infiltration and in some areas necrosis. The intima and the inner elastic membrane were disorganized and distorted. In those thrombosed, the lumen was narrowed owing to edema and thickening of the walls.

The experiments showed that a properly adjusted clamp could be left in position, closing the artery for from 24 to 48 hours, without serious injury to the walls.

*Physiologic:* The immediate effect on the circulation of temporarily closing one carotid artery was to increase the blood-pressure, but usually a compensation followed, and the pressure returned to its normal level. No effect upon the respiration was observed. Simultaneously closing both carotid arteries produced a greater rise in the blood-pressure, which by physiologic compensation usually soon returned to the normal level. In many of the experiments there was a decrease in the respiratory action, although the effect was very slight. In no instance were there any striking results noted. In the recovery experiments in the cases in which the clamps were allowed to remain on the arteries, closing them and the wound pursuing an aseptic course, no effect upon the animal was observed beyond that attributable to the anesthesia and the operation. The animals seemed playful and strong. Even after 24 hours of complete closure there was not much microscopic evidence of injury to the vessel wall. The circulation through the clamped portion was readily re-established. However, in cases in which, during the application of clamps for a considerable length of time, say two days, the animal in the meantime had suffered infective inflammation of the wound, the damage of the vessel walls was very considerable and the lumen was in some instances occluded. As to the after effects, in no case was there clotting; the aseptic cases made good recoveries; the circulation was re-established; and no impairment of consequence was observed. The circulation of the brain was carefully observed at the post mortem, and in no case was either emboli or thrombi found, or any effect on the brain noted. After considering several devices, the most accurate, efficient, and safe one seemed to be that of applying a clamp, so constructed that its blades could be adjusted by means of a set screw, and when they were approximated so as to close the vessel, but not compress its walls, the blades were parallel to each other. One blade was made longer than the other, and its end turned up so as to prevent the escape of the artery. Over these blades were stretched pieces of rubber tubing, thereby minimizing the effect of contact with the vessel wall. In applying the same, it is necessary to bear in mind that the walls need only be approximated, not compressed. The adjustable screw gives so perfect a mechanical control of the lumen of the vessel as to enable the surgeon to perform the operation and secure the bleeding vessels with a minimum loss of blood.

CLINICAL APPLICATION

**A NEW METHOD OF CONTROLLING HEMORRHAGE IN CERTAIN OPERA-
TIONS ON THE HEAD AND NECK**

*Technique:* Twenty minutes previous to making the incision
one one-hundreth of a grain of atropin should be injected, in
cases in which the technique is likely to involve the trunks of the
vagi or their superior laryngeal branches, for the purpose of
preventing possible inhibitory action upon the heart. Each com-
mon carotid artery is closed by means of a small clamp, whose
blade is long and protected by a thin rubber tubing. The lower
blade is slightly longer than the upper, and turns up at its free end
so that its grasp upon the artery will be more secure. The spring
end of the clamp is so arranged that when the blades are closed
sufficiently to approximate the walls of the vessels they become
parallel. The closing of the blade is accomplished by an adjust-
able thumb screw, making definite closure. In operations in which
blood may enter the pulmonary tract, the patient should be placed
in a Trendelenburg posture. This partially compensates the low-
ered cerebral blood-pressure resulting from closing the carotids.
While this posture somewhat increases the venous and capillary
hemorrhage, the increase of the venous pressure diminishes the
danger of the entrance of air into the larger venous trunk, should
they accidentally be injured. Fortunately venous and capillary
hemorrhages, except in cases involving the larger veins, are rela-
tively of little consequence. On completion of the operation, in
cases in which the Trendelenburg posture is employed, it is safer
to restore the patient to the horizontal position before releasing
the carotids, as in the inclined posture the normal blood-pressure
of the brain is increased by the mechanical factor, and releasing
the clamps in this position would raise the pressure above the
normal. The release of the clamp should be made slowly while
inspecting the field of operation to detect any vessels that might
have been overlooked. The control of the arterial hemorrhage
is absolute, except in such vessels as received direct collateral
pressure from the vertebral arteries. According to the researches
of Bayliss and Starling, there are no vasomotor nerves supplied
to the vessels of the brain. The circulation being mechanical,
the blood-vessels of the brain should be more favorable to the
employment of such technique than the vessels of almost any
other organ of the body in which the blood supply is more or
less regulated by the vasomotor mechanism.

CASE 1: Both common carotids closed. Recovery. Operation was performed January, 1897.

The patient upon whom this technique was employed was a colored man, 46 years of age, admitted to St. Alexis Hospital on account of a large fibrosarcoma filling the mouth so as to render its complete closure impossible. Breathing was so obstructed as to threaten suffocation, and at night was so heavy and labored that it could be heard at a considerable distance. Under cocain, tracheotomy was performed for the double purpose of removing the danger of asphyxia and as a part of the technique to be employed. Aside from emaciation from the necessary liquid diet, the patient was in good condition. The tumor was first observed six years previous in the posterior part of the hard palate. A year later it was removed, but recurred, and had been growing since that time. On account of its size, the extent of its attachments, when I first saw him, could not be determined. Its translucent surface displayed a rich supply of blood-vessels, some of considerable size. In the operation the technique here described was employed. The tumor was delimited by an incision in the healthy mucous membrane. The hard palate was divided along this line. The vomer was severed along the floor of the nose and the entire mass turned out. After the necessary revision of the wound the principal vessels were secured, and everywhere the wound was touched with the thermo-cautery. After the operation had been completed, the wound dressed, and perhaps 10 minutes had elapsed, respiration suddenly failed. Artificial respiration was maintained during 25 minutes. The application of ice, alternated with a brisk rubbing with a warm towel, proved an efficient stimulus to respiration. The entire mouth was packed with iodoform gauze, which was allowed to remain for 24 hours, after which boric acid solution with sufficient thymol to correct the disagreeable odor was used in a mouth wash. The tracheal tube was removed after two weeks, when it was thought that the danger of pulmonary infection had passed. The patient was soon able to leave his bed, and made an uneventful recovery. Four years later there was no recurrence.

CASE 2: Removal of a large congenital tumor of the neck. Closure of both common carotid arteries. Recovery.

Female, 21 years of age. At birth it was large and more developed on the right side than on the left, greatly increasing in size as she grew older. At the time of operation the tumor occu-

pied the entire anterior and much of the latter portion of the neck. On the left side it extended past the line of the ear. On the right, over the border of the sternomastoid muscle. It extended from the sternum to the chin. The whole tumor was very large and pendulous. There was free discharge of a glairy mucus from several sinuses. In these sinuses a probe could be passed down to the level of the larynx. The tumor mass was of varied consistency, at places cystic and moderately fluctuating, at others giving the resistance of fleshy tissue. The sinuses did not communicate with the interior of the larynx. A laryngoscopic examination showed that the trachea was markedly flattened in its antero-posterior diameter. Both voice and respiration were impaired. The danger of hemorrhage was so great that the patient had previously been advised against operation.

*Operation:* The carotid arteries were found pressed back against the vertebral column. They were closed by means of the clamps, after which the operation was carried out almost bloodlessly. The only blood-loss was in making the incisions in the portion supplied by the inferior thyroid arteries, which were not closed. When the common carotid arteries were clamped, the face became blanched and the pulse disappeared from all portions of the head. In experiments on animals we have been able to show that the intracranial pressure is kept sufficiently high for the functioning of the bulbar centers by the vertebral arteries alone. If, however, the closure of the common carotids is permanent, cerebral softening is likely to ensue; if temporary, untoward effects follow. The patient made a good recovery, and there is ' but a minimum scar on the neck. Both of the external jugular veins were excised with the tumor. All of the deeper structures were laid bare.. The tumor was in anatomical relation with the sheaths of the common carotid arteries, the trachea, the larynx, and all the deeper structures of the neck. There was no capsule. At first I was inclined to believe that one of the recurrent laryngeal nerves was sacrificed. She spoke in stridulous tones. Later the voice cleared.

CASE 3: Clamping of both common carotids; partial resection of the tongue; removal of the floor of the mouth; excision of the submaxillary and sublingual glands; resection of the parotid; excision of the superficial and deep cervical lymphatics on the left side; excision of the jugular vein; resection of the buccal aspect of the inferior maxillary bone. Recovery.

*Diagnosis:* Typical epithelioma situated on the floor of the mouth, extending from the left side of the tongue to the inferior maxilla. Slight enlargement of several lymphatic glands could be palpated. Age 48; previous health good; obese and plethoric: weight 236 pounds: neck short, thick and fat.

*Operation:* Chloroform-morphin anesthesia. One one-hundredth grain of atropin was given half an hour before the operation to prevent cardiac inhibition from probable mechanical irritation of the superior laryngeal or of the vagus. Both common carotids were closed by means of the rubber-tipped screw clamps. The incision on the right side being an inch long, fibres of the sternomastoid were separated. On the left side the vessel was secured in a like manner. The incision was carried upward, then outward, parallel with the jaw to the parotid gland, and an inner incision was carried to the median line. Reflecting the skin exposed the entire cervical field. The superficial chain of glands was first removed, then the deeper. The submaxillary gland was encroached upon by a metastasis of the adjacent lymphatics, and was accordingly removed. Metastases were found in the deep cervical, in the parotid region, and along the jugular vein. The jugular together with the glands was excised. While dissecting out the deeper glands the pulse increased rapidly to 162, due to increased stimulation of the sympathetic, while the vagal action was prevented by the atropin. The cause being recognized, no stimulation was given. The pulse soon returned to the previous rate. The extensive cervical dissection was then packed with gauze. The tongue was held well over and the mouth lightly packed with gauze. The base of the tongue, the entire floor of the mouth on the left side, and about half of the adjacent jaw was removed. The resection of the tongue included about one-third of its left half and base. There was free communication between the mouth and neck.

The clamps were now gradually unscrewed and the circulation of the mouth, face and neck re-established. The absolute control by means of the screw clamps made it possible to secure all the bleeding points without appreciable blood-loss. There was but a trifling hemorrhage, mostly venous, and the operation was greatly facilitated by keeping a bloodless field. The patient made a rapid recovery. There were no unfavorable symptoms due to the closure of the carotids either during the operation or after it.

CASE 4 (Abstract): Temporary closure of common carotid. Removal of sarcoma of parotid; vagus exposed; external carotid and jugular tied; cardiac inhibition from vagal and laryn-

geal irritation; application of 2% solution of cocain prevented further inhibition. Recovery.

The common carotid was closed by means of special clamp; the jugular vein and the external carotid was excised; the vagus was laid bare. On account of an insufficient dose of atropin, irritation of the vagus while separating it reduced the heart-beats from 92 to 56. The nerve being exposed, cotton saturated with a 2% solution of cocain was packed around it. Although it became necessary to inflict greater mechanical irritation in the further dissection than had been previously inflicted, the heart promptly returned to 90 and was not further affected. Cocain blocked the afferent impulses and protected the heart. Quick recovery followed.

CASE 5 (Abstract): Excision of the tongue, left floor of the mouth, middle half of the jaw, glands of the neck, submaxilla, and a portion of the parotid glands *en bloc* for carcinoma. Recovery.

Male, aged 58; preliminary tracheotomy one week before the operation. Both common carotids closed by means of the clamp. One one-hundredth grain of atropin given. Incision carried along the large vessels in the neck, exposing them, to the angle of the jaw, then upward to the base of the jaw; another incision parallel to the jaw. Skin flaps directed in all directions. Large vessels exposed at the base of the neck. All the glands and fascia removed up to the jaw. Jaw sawed through at two points, after which the entire tongue, floor of the mouth, and left tonsil were removed with the scissors. The pharynx had been previously packed with gauze. There was but a trifling hemorrhage. The patient's pulse-rate never changed during the operation which was completed in 30 minutes. The closing of the common carotid arteries afforded a bloodless field so far as capillary and arterial hemorrhage was concerned, and but slight from the venous sources. The atropin paralyzing the terminals of the vagus prevented any inhibition. Patient made a rapid recovery.

CASE 6 (Abstract): Carcinoma arising from the duct of the parotid gland. Excision; closure of the common carotid. Recovery.

Female, aged 42; in good physical condition. During the operation the large vessels and the upper portion of the vagus and the superior laryngeal were exposed. Although the patient had been given one one-hundred and twenty-fifth grain of atropin the pulse was reduced during the manipulation of these structures

from 90 to 52. A piece of cotton saturated with a 2% solution of cocain was packed down upon the nerve, after which the pulse returned to its previous rate in less than a minute. The operation was completed, involving continuous manipulation of the vagus and the superior laryngeal, with no effect upon the heart's action. The respirations were shortened and deepened.

CASE 7 (Abstract): Operation for tubercular glands of the neck. Dissection involved the jugular, deeper vessels, and the vagus nerve; cardio-inhibitory action from manipulating the vagus. Recovery.

Patient eight years old. While separating the glands from the vagus in its upper portion near the parotid the heart-beats dropped from 92 to 62. The field was kept bloodless, so that all the structures could be seen. The vagus had been laid bare. A 2% solution of cocain was applied upon the nerve, and the pulse went up immediately to 90, after which, although the dissection involved the nerve more than before, no inhibition was noted.

CASE 8 (Abstract): Closure of the common carotids. Physiologic dosage of atropin; laryngeal application of cocain; excision of the tongue, epiglottis, left tonsil, floor of the mouth, lower jaw, submaxillary and parotid glands, left jugular vein, left external carotid artery, and the vagus nerve; but little shock. Easy immediate recovery. Death from secondary hemorrhage on the 13th day.

Patient had had six operations for epithelioma; the disease originated in the floor of the mouth. The operations and the disease had so far destroyed the jaw and the soft parts that the patient was with increasing difficulty able to eat. The cicatricial and carcinomatous contractions and hardening fixed the lower jaw and was progressively closing the mouth. The procedure was recommended after consultation with distinguished surgeons. The preliminary preparations having been made, an incision was carried from each angle of the mouth outward and downward in relation to the growth. The jaw was disarticulated on the left side, while on the right it was severed in the upper portion of the ramus. The extent of the external part of the operation was indicated by a free skin incision. The jaw was severed first on the right side, then on the left. The tongue, tonsil, and the floor of the mouth were then severed lateraly and posteriorly, after which, by continuing the dissection along the vertical plane of the esophagus, larynx and trachea, all the structures, including the parotid, submaxillary and sublingual, and regional lymphatic glands, were removed. The dissection then passed through the

plane of the carotid artery, jugular vein, and vagus on the left side, all of which were included in the parts removed. Especial care was taken in securing the veins. The epiglottis showing a tendency to close, the larynx in a light valve-like manner was excised. The removal *en bloc* by carrying the dissection along the planes indicated not only facilitated dissection, but insured the removal of all the local carcinomatous tissue.

The patient bore the operation well, exhibiting a pulse rate of 96 at the close of the operation and good respiratory rhythm. On opening the arteries the circulation of the head was quickly restored and consciousness almost immediately regained. The patient progressed favorably until the 13th day, when death from secondary hemorrhage occurred.

The absolute control of the blood supply by means of the special device, thereby maintained a clear field for dissection; the prevention of cardiac collapse through either direct or reflex inhibition by the administration of a physiologic dosage of atropin; the prevention of reflex inhibition of respiration by the application of cocain upon the laryngeal mucosa, places even so extensive an operation on a safe basis so far as the immediate operative effects are concerned.

CASE 9 (Abstract): Infant, seven months old; had an angio sarcoma of the cheek and neck of rapid growth and great vascularity. Common carotids closed by means of special mechanism. Removal of the entire growth. Recovery.

The extensive development of the tumor and frailty of so young a subject almost precluded any operative procedure, but on account of the assurance of a safe and absolute control of the blood supply an excision was attempted. Both the common carotids were closed. The blood supply was absolutely controlled, and the dissection could be made in a clear field without loss of blood. The tumor had invaded the structures of the cheek, extending down to the mucous membrane, and in the neck extending well down below the angle of the jaw, involving the parotid region. After removing the entire growth it was impossible to bring the parts closely together. Repair was rapid and the child made an uneventful recovery, the operation having been well borne.

CASE 10 (Abstract): Carcinoma of the septum of the nose. Excision. Closing both common carotid arteries.

Operation was performed bloodlessly, involving the temporary lateral resection of the entire nose, extending to the posterior nares, the base of the skull. Hemorrhage entirely controlled. Nose was replaced. Good recovery.

CASE 11 (Abstract) : Excision of one half the tongue, the floor of the mouth, submaxillary glands, entire chain of lymphatic glands, extending along the jugular and angle of the jaw. Excision of the jugular vein. Recovery.

Preliminary tracheotomy. Both carotid arteries closed; fairly bloodless field excepting a small amount of venous hemorrhage. There was not even an appreciable alteration in the pulse and respiration. Patient made a good recovery.

### CONCLUDING REMARKS

The proper interpretation of a slowed or of an accelerated pulse, or of an inhibited respiration, the prevention of either direct or reflex inhibition of the heart from mechanical stimulation of the vagus or of its branches by the use of atropin and cocain, the safe and absolute control of hemorrhage by temporarily closing the carotid arteries render operative procedures of the head and neck so much safer as to greatly increase surgical possibilities.

# OBSERVATIONS ON THE ORIGIN AND OCCURRENCE OF CELLS WITH EOSINOPHILE GRANULATIONS IN NORMAL AND PATHOLOGICAL TISSUES.

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(PLATE VIII.)

In the routine examination of 825 specimens derived from operations, and of the organs from 120 autopsies from the various services of Lakeside Hospital, we have been struck with the frequency with which cells with eosinophilic granulations have been found. It is our purpose in this article to classify and analyse these observations.

By the terms "eosinophile and eosinophilic cell," and "cell with eosinophilic granulations" as used in this article, we mean a cell with coarse or moderately coarse granulations which stain deeply and intensely with acid dyes, especially with eosin. These cells correspond to the eosinophilic cells of human blood of Ehrlich, and to the coarsely granular oxyphile cell of Kanthack and Hardy. All cells with homogeneous non-granular protoplasm, as well as the polymorphonuclear neutrophilic cell of Ehrlich or the finely granular oxyphilic cell of Kanthack and Hardy, are excluded from consideration.

*Methods.*—Most of the tissues upon which this study is based were hardened in Zenker's fluid, some in Orth's fluid, and a few in 95 per cent alcohol. The best results were obtained with Zenker's fluid. Celloidin was commonly used for embedding, though the paraffin method was used in some cases. As a matter of routine sections were stained in haematoxylin followed by a rather strong aqueous solution of eosin which was allowed to act for a short time. Overstaining with eosin was studiously avoided. In most cases there was no intention of staining for eosinophilic granulations, but the sections were stained in the usual manner by a number of different workers from the various services of the

hospital. Sections from a number of cases were stained with eosin followed by methylene-blue, which gave good results. Besides eosin in special cases other acid dyes, such as acid fuchsin and picric acid combined (Van Gieson's stain) the Biondi-Heidenhain and the Ehrlich triacid stains, were tried and always with positive results.

Sections which showed large numbers of eosinophiles were treated with freshly-prepared ammonium sulphide for from six to twenty-four hours but in no case were any of the granules changed in color. Sections treated with fresh potassium ferrocyanide also failed to show the presence of iron.

For convenience we shall classify our observations as follows:

Observations on the presence of cells with eosinophilic granulations in (I) apparently normal organs (II), in pathological tissues in material derived from operations, (III) in organs showing pathological changes in cases coming to autopsy.

### I. Cells with Eosinophilic Granulations in Apparently Normal Organs.

In ten normal appendices these cells were numerous; in five cases they were confined to the stroma of the mucosa, in two they were in both the stroma and in the lymphoid tissue, while in three they were numerous in the stroma with a few in the capillaries. A few eosinophiles were found in the blood-vessels of a normal Fallopian tube.[1]

They were found in apparently normal organs in the following cases coming to autopsy:

*Case I.* A few polymorphonuclear eosinophiles were present in the kidney of a five days old infant with omphalitis and *Staphylococcus aureus* bacteriaemia.

*Case II.* A child one month old, dead of streptococcus infection. A few polymorphonucler eosinophiles were present in the mucosa of the ileum.

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[1] Since the above was written we have examined a large number of both normal and inflamed appendices, in nearly every one of which there were large numbers of eosinophiles. In the normal appendix they are confined to the interglandular stroma and the lymphoid tissue, while in inflammation they invade all coats. They are much more readily found after hardening in Orth's or Zenker's fluids than in alcohol.

*Case III.* In a still-born child, seven months in utero, the liver capillaries contained large numbers of polymorphonuclear eosinophiles.

*Case IV.* In a child with imperforate anus, dead three days after birth, the muscularis of the rectum at the point of atresia showed numerous round cells, and a few polymorphonuclear eosinophiles.

*Case V.* In a case of epidemic cerebro-spinal meningitis, due to *Diplococcus intracellularis meningitidis,* a few polymorphonuclear eosinophilic cells were seen in the stroma of the mucosa of the small intestine.

*Case VI.* In a case of a child two days old, in whom death followed gastro-intestinal haemorrhage, due probably to haemophilia, polymorphonuclear cells with eosinophilic granulations were found in numbers in the connective tissue of the portal spaces in the liver.

*Case VII.* In a child two weeks old, dead of follicular dysentery and omphalitis, the latter due to *Staphylococcus pyogenes aureus,* there was marked congestion of all the organs, including the thymus. The lymphoid tissue of the latter organ contained large numbers of coarsely granular eosinophiles. A few of these cells had small deeply staining reniform or polymorphous nuclei. Most of them, however, had a single round, oval, or reniform slightly vesicular nucleus resembling in all respects the nucleus of the plasma cell. The nuclei of many of these cells were eccentric. In some plasma cells nuclear figures were seen.

There was no special relation of the eosinophiles to Hassal's bodies. The eosinophiles were most numerous at the peripheral portions of the glands.

In four of the seven cases there was infection, septicaemia occurring in two. In these four cases the infectious agent may have stimulated the formation of the eosinophiles.

## II. Cells with Eosinophilic Granulations in Pathological Tissues in Material Derived from Operation.

In twelve cases of acute appendicitis, these cells were numerous in the tissues of five, in the tissues and vessels of one, and very numerous in the tissues and vessels of two, and very numerous in the tissues in four.

In six cases of chronic appendicitis, a few were found in the tissues and exudate in two, and in the other four they were numerous in the tissues.

In six cases of salpingitis, one of which was tubercular, a few were found in the stroma of the mucosa and in the muscularis. In four cases a few occurred in both vessels and tissues, in six cases there were a few in the blood-vessels, and numbers in the tissues; in eight cases they were numerous in the tissues and absent from the blood-vessels; in eight cases they were numerous in both vessels and tissues; in one case they were numerous in the vessels and very numerous in the tissues; in two cases they were very numerous in the tissues and absent from the blood-vessels; in one case they were very numerous in both vessels and tissues, and in one case they were present in small numbers in the vessels and in great numbers in the tissues, making thirty-seven cases of salpingitis in all.

In one case of acute ovarian abscess they were present in small numbers in the tissues, while of eight cases of chronic ovarian abscess they were present in the tissues in small numbers in one case, in large numbers in two cases, and in great numbers in four cases, but were absent from the blood-vessels, while in two cases they were present in great numbers in both tissues and blood-vessels.

In two cases of acute perioophoritis they were present in both vessels and tissues in large numbers. In four cases of chronic perioophoritis they were present in the tissues in small numbers in one case, in large numbers in another case, in very large numbers in a third case, while in the last case they occurred in small numbers in the blood-vessels and in large numbers in the tissues.

In two corpus luteum cysts they were numerous in the tissues in one case, present in small numbers in the vessels and very numerous in the tissues of the other.

In one case of congestion of the Fallopian tube they were present in numbers in the blood-vessels.

In a case of inflammatory thickening of the broad ligament they occurred in numbers in both blood-vessels and tissues.

In one case of hypertrophic endometritis a few were found in the tissues, and in a case of acute interstitial endometritis after abortion, a few were present in the blood-vessels and large numbers in the tissues.

In three cases of carcinoma uteri they occurred in one case in numbers in both vessels and tissues, in the other two cases in great numbers in the tissues while none were found in the blood-vessels.

In two cases of epithelioma of the vagina numbers were found in the tissues in one case, a few in the vessels and great numbers in the tissues in the other case.

In one *Staphylococcus aureus* abscess of the gland of Bartholin numbers were found in the tissues but none in the blood-vessels.

Two cases of proctitis showed very large numbers in the tissues.

One case of pilonidal abscess showed numbers in the tissues, but none in the vessels.

In three cases of omentitis one showed numbers in the tissues, but none in the vessels, the second, numbers in both blood-vessels and the tissues and in the third none in either the vessels or the tissues. In one case each of carcinoma of the arm, secondary epithelioma of a lypmh gland, epithelioma of the scrotum, and in two cases of epithelioma of the face they were found in the tissues in numbers. They were present in the tissues in varying numbers in cases of tuberculosis involving the following organs: striated muscle, anus, rectum, ureter, cervical lymph glands, and skin. In three nasal polyps numbers of eosinophiles were present in the tissues in two and in the tissues and blood-vessels in one. They were numerous in the lesions in six cases of osteomyelitis, three of which were tuberculous. They were found in considerable numbers in the tissues in one case of gonorrhoeal lymphangitis and in a gumma of the skin.

For comparison with the foregoing some fifty cases of inflammatory and other lesions of various tissues were noted in which eosinophiles were absent. Among these there were twenty cases of acute and chronic salpingitis, three cases of abortion remnants, three of endometritis, and several corpus luteum cysts.

Altogether coarsely granular eosinophiles were present in either the tissues, exudates or blood-vessels in 108 out of 825 consecutive specimens derived from operation, or in 13.09 per cent of the cases; 80 of these cases were inflammatory, 24 being acute and 56 chronic. Appendicitis was the lesion in one-half of the acute cases. There were 9 cases of tuberculosis and 9 of syphilis; 9 of the 16 non-infectious cases were carcinomata and 3 were nasal

polyps. We have never found eosinophiles in other tumors except in one case of lymphosarcoma [2] (Case XX).

Of the 108 cases 74 per cent were inflammatory and counting the cases of tuberculosis and syphilis 83.3 per cent were infectious processes.

These observations show that these cells are frequently present and probably take an active part in inflammatory lesions. Eosinophiles were found in greatest numbers in appendicitis, pyosalpinx, chronic ovarian abscess, and carcinoma. They were almost always associated with plasma cells, which were often very numerous. Polymorphonuclear neutrophiles were not numerous as a rule, but in some cases, in salpingitis especially, they were abundant.

There is a close relation between the occurrence of eosinophiles and plasma cells. In many cases (as will be hereinafter described), especially in appendicitis, the transition of plasma cells into eosinophiles was readily traced. In appendicitis the eosinophiles normally present in the stroma of the mucosa and in the lymphoid tissue are markedly increased in number and wander into the inflamed areas. In chronic appendicitis they are commonly seen in great numbers in the muscularis. In carcinoma they are sometimes seen in the blood-vessels, but even here they are closely associated with plasma cells. In a large number of cases of salpingitis, on the other hand, numbers of eosinophiles were present in the blood-vessels as well as in the tissues. In salpingitis eosinophiles were found in greatest numbers in the mucosa and in the muscularis, and but rarely in the serosa or in the lumen of the tube. There is evidence, then, that in salpingitis some of the eosinophiles in the exudation are derived from the blood-vessels. We are informed, however, by Dr. Weir, the Resident Gynaecologist, that in a number of the cases of salpingitis operated on in Dr. Robb's service showing a decided leucocytosis (of the polymorphonuclear neutrophiles) before operation, a differential count of the leucocytes always failed to show eosinophilia, even in the cases in which eosinophiles were found in large numbers in the pelvic lesions. The consideration of the bacteriology of these cases will be postponed to the end of the article.

[2] In a recently examined case of giant cell sarcoma of the mediastinal glands invading the pectoral muscles there were great numbers of eosinophiles in the tumor and in the neighboring muscle.

*Description of the Eosinophilic Cells met with in the above series.*

In the apparently normal tissues the stroma of the mucosa of the appendix, ileum, and stomach, for instance, by far the majority of the eosinophilic cells corresponded in all respects to those commonly found in the circulating blood. They had horseshoe-shaped, or trilobate nuclei, surrounded usually with coarse granules which stained deeply with eosin. In some of these cells, however, the granules were finer than in others. The cell outlines were often irregular. Besides these cells a few were seen with single, usually round, deeply-staining nuclei, surrounded, some by finely granular, others by coarsely granular protoplasm. Both varieties of granules stained deeply with eosin. These cells were about the same size as the large mononuclear cells with hyaline protoplasm. The nuclei of the two varieties of cells were identical in appearance, with the exception that the nuclei of the eosinophilic cells commonly stained more deeply than those of the large hyaline cells of the blood. In the second series of cases, in which eosinophilic cells were found in inflammatory and other lesions, these cells were in the main similar to those found in the apparently normal organs, with the exception that mononuclear cells were present in larger proportion in the former than in the latter.

In some of the inflammatory cases, notably in ovarian abscesses and in pyosalpinx the eosinophilic cells were very numerous in the tissues. As a rule, few polymorphonuclear neutrophilic cells were present with the eosinophiles, except in acute cases, where the former were usually very numerous, and the latter few in number. Elsewhere these two varieties of cells were not commonly seen together. In the chronic cases as a rule, and often in the acute cases, especially in ovarian abscess and pyosalpinx, the eosinophiles were associated with plasma cells, which were present in large numbers. In only a few cases were the eosinophilic cells the most numerous in the exudation.

III. Cells with Eosinophilic Granulations in Organs showing
    Pathological Changes in Cases coming to Autopsy.

In the ten following cases cells with eosinophilic granulations were found in the spleen, in association with chronic interstitial splenitis, and in various other organs.

*Case VIII.*   Male, aged 60 years.   Interstitial splenitis with polymorphonuclear eosinophiles in fairly large numbers in the spleen pulp; carcinoma of the pancreas and liver.

*Case IX.*   Male, aged 45 years.   Congestion of the spleen with haematoidin in the trabeculae, eosinophiles in clumps of three and four in the splenic pulp.   Death from intestinal obstruction.

*Case X.*   Female, aged 3 years.   Pleuropneumonia with serous effusion, interstitial splenitis, persistent thymus, healed eczema, eosinophilic cells in the splenic pulp and in the thymus. The thymus measured 5 x 3 x 2 cm. and was of ordinary appearance on section.   The spleen weighed 25 gm. and measured 7 x 5 x 2 cm.   The capsule was adherent to the diaphragm over an area 1 x 1 cm.   On section the consistency was increased, the Malpighian bodies and trabeculae were both well marked.   The outlines of sections of the spleen were serrated, the depressions corresponding to the very thick trabeculae.   Beneath the capsule there were broad and narrow bands of connective-tissue thickening.   In the pulp here and there, polymorphonuclear eosinophilic cells were found in considerable numbers.   In many of the smaller arteries there was an obliterative endarteritis, while the media of many was hyaline.   There was no round cell infiltration.

In sections of the thymus the lobule as well as Hassal's bodies were well marked.   The interlobular stroma was normal.   Large numbers of polymorpho- and mononuclear cells with eosinophilic granulations were seen in the lobules, in the interlobular connective-tissue and in the blood-vessels.

*Case XI.*   Male, aged 5 years.   Bronchopneumonia with general infection with *Bacillus mucosus capsulatus;* eosinophiles in the spleen and thymus.

Sections of the spleen showed marked congestion with numerous eosinophiles in the pulp.   The thymus showed marked congestion with many eosinophiles (mostly mononuclear) in the lymphoid tissue; in many places they were very numerous about the bodies of Hassal.

*Case XII.*   A still-born child at full term, with hydrocephalus and meningocele; eosinophiles in the spleen and thymus.

Sections of spleen showed marked congestion of the vessels of the pulp in which a few polymorphonuclear eosinophiles were seen.

The thymus was much congested and showed a moderate number of eosinophiles in the lymphoid tissue.

*Case XIII.* Male, aged 4 months. Bronchopneumonia; malnutrition; eosinophiles in the liver, spleen, ileum, colon, thymus and lymph glands.

Sections of the liver showed a number of plasma cells and a few polymorphonuclear eosinophiles in the vessels; the spleen showed large numbers of the same cells in the pulp. The small and large intestines, the thymus and the mesenteric lymph glands showed large numbers of eosinophiles, both mononuclear and polymorphonuclear, in the lymphoid as well as in the interstitial tissues.

*Case XIV.* Male, aged 5 years. Burns of the third degree; chronic interstitial splenitis; eosinophiles in the liver, spleen, adrenals, thymus, mesenteric lymph glands, and gastro-intestinal tract; persistent thymus.

Sections of the spleen showed congestion and diffuse increase of fibrous tissue, with a large number of mono- and polymorphonuclear eosinophiles scattered throughout the pulp, which contained large numbers of typical plasma cells. Every stage of transition between plasma cells and eosinophiles could be made out. The liver showed marked congestion of the capillaries with cloudy swelling of the liver cells; polymorphonuclear eosinophiles were found in the capillaries of the liver and adrenals, the lymphoid tissue of the thymus showed large numbers of the same cells; the mesenteric glands showed congestion and hyperplasia with large numbers of eosinophiles in the lymphoid tissue.

*Case XV.* Female, aged 40 years. Streptococcus bacteriaemia following pelvic abscess; interstitial splenitis with eosinophiles in the spleen, liver and abscess wall. Sections of the spleen showed marked congestion and increase of fibrous tissue with a moderate number of mono- and polymorphonuclear cells in the pulp; a few of the same cells were present in the blood-vessels of the liver. In sections of the abscess wall there were large numbers of streptococci, numerous mononuclear and polymorphonuclear eosinophiles, plasma cells and neutrophiles.

*Case XVI.* Male, aged 45 years. Empyaema and lobar pneumonia; interstitial splenitis with eosinophiles in the lung and spleen.

In sections of the pneumonic area the alveoli were filled with masses of fibrillated fibrin containing polymorphonuclear neutro-

philes. In some alveoli there were large globular polypoid masses of fibrin attached to the alveolar walls by narrow bases and containing fibroblasts and capillaries. In many of the alveoli and in some of the alveolar walls numerous polymorphonuclear eosinophiles were seen. The spleen showed diffuse connective-tissue increase with a few polymorphonuclear eosinophiles and many plasma cells in the pulp.

*Case XVII.* Male, aged 35 years. Miliary tuberculosis of the lungs with some mononuclear eosinophiles in the granulation tissues about the tubercles; diffuse interstitial splenitis with polymorphonuclear eosinophiles in the pulp; general chronic passive congestion; malaria (tertian form). Coverslips made from the spleen showed dark pigment in the leucocytes and a number of red blood-cells containing malarial parasites of the tertian type. Sections of the left lung showed chronic interstitial pneumonia, with fibrous tubercles. The tuberculous tissue was rich in plasma cells, polymorphonuclear neutrophiles and mononuclear and polymorphonuclear eosinophiles. The spleen showed marked congestion, a large amount of haematoidin in the trabeculae, and interstitial splenitis with a large number of polymorphonuclear eosinophiles in the pulp.

Five of the foregoing cases were young children (Cases X, XI, XII, XIII, XIV) and all showed large numbers of eosinophiles in the thymus as well as in the spleen. Case XIV is of special interest as the formation of eosinophiles was in active progress, and these cells were present in increased numbers in the various organs, as well as in the tissues of the spleen, thymus (persistent), lymph glands and intestines. Besides their occurrence in the spleen in the five remaining cases, they were also found in one case in the wall of a pelvic abscess (Case XV), in one case in the exudate of lobar pneumonia (Case XVI), and in one case in tuberculous areas in the lungs (Case XVII). In two cases they were present in all the organs except the heart and lungs. Although circulatory eosinophilia has been described in malaria, as far as we have been able to learn, Case XVII is the first one in which these cells have been observed in the spleen in this disease.

In the next four cases cells with eosinophilic granulations were present in large numbers in the gastro-intestinal tract.

*Case XVIII.* Male, aged 51 years. Atrophic cirrhosis of the liver and gastric mucosa, with eosinophiles in the stroma of the latter. Sections of the stomach showed atrophy of the glands, and infiltration of the stroma with numerous mono- and polymorphonuclear eosinophilic cells.

*Case XIX.* Male, aged 34 years. Arsenic poisoning; polymorphonuclear eosinophiles in the intertubular tissue of the gastric mucosa. Sections of the stomach showed some loss of the surface epithelium and marked dilatation of the blood-vessels of the mucosa. There was no special destruction of the tubules. The intertubular tissue contained numbers of plasma cells and polymorphonuclear eosinophiles. The epithelial cells of the tubules were often separated from the basement membrane, and there was marked congestion of the submucosa.

*Case XX.* Male, aged 64 years. General lymphosarcoma with numerous mono- and polymorphonuclear eosinophiles in the stroma and muscularis of the small intestine. Sections of the spleen, liver, kidneys, intestines and mesenteric glands showed lymphosarcoma. Sections of the duodenum and jejunum showed loss of the superficial epithelium of the mucous membrane of some of the glands, with numbers of large bacilli (*B. aërogenes capsulatus*) in the degenerated areas. In the muscularis and to a less degree in the stroma of the mucosa, a large number of cells with eosinophilic granulations were seen. These cells were of several types, and showed distinct transition forms. In the stroma of the mucosa the cells were all of one type. They had rather large, pale nuclei, and were similar in every way to plasma cells, except for the eosinophilic granulations. There were a moderate number of plasma cells in association with the eosinophiles. In the muscularis the picture was materially different. Here the prevailing type of cell had a small, very dense eccentric nucleus, round, oval or elongated, and an irregular cell body, which conformed itself to the clefts between the muscle fibres, and consequently showed a great variety of shapes; the granulations were extremely coarse, and crowded closely together. Besides these there were a number of cells similar to the above except that the nuclei were somewhat vesicular, and contained small clumps of chromatin. These forms were the most common ones, but there were also a fairly large number of ordinary polymorphonucler eosinophiles with double,

horse-shoe, or trilobate nuclei. Besides these there was a great variety of forms which were apparently transitional between the smooth muscle cell of the intestine, and the typical, fully-formed polymorphonuclear eosinophile. There were cells with double or even trilobate nuclei, but without a trace of nuclear detail, and others whose nuclei were markedly vesicular. The eosinophiles apparently had a double origin, arising on the one hand from the plasma cells which were present in both the stroma of the mucosa and in the muscularis, and on the other, from the muscle cells. Eosinophiles were present also in the capillaries and in the small veins, but were infrequent in the larger vessels. Only two types occurred, the ordinary polymorphonuclear form, and the mononuclear form with a vesicular nucleus. The forms with dense nuclei were entirely absent from the vessels. No polymorphonuclear neutrophiles were seen in the tissues.

*Case XXI.* Male, aged 34 years. Extensive ulceration of the rectum, sigmoid flexure and descending colon, with polymorphonuclear eosinophilic leucocytes in the large intestine and in the spleen; taenia saginata in small intestine. There was an extensive suppurating wound on the left thigh, communicating with the sigmoid. The rectum, sigmoid and colon up to the splenic flexure were the seat of larger and smaller ulcers with granulating bases and margins. Over large areas of the intestine the mucosa was lost, the surface being covered with granulation tissue.

The spleen weighed 180 gms., and measured 12 x 6 x 4 cm. The capsule was smooth; on section the organ was dark red in color, the consistency was normal. The trabeculae were prominent, the Malpighian bodies obscure. Microscopically the trabeculae were thickened, and there was a diffuse increase of connective-tissue in the pulp, with numbers of polymorphonuclear cells with eosinophile granulations. The capillaries contained a large number of polymorphonuclear neutrophilic leucocytes. In the granulation tissue of the rectum and sigmoid, in addition to fibroblasts, plasma cells and polymorphonuclear neutrophilic leucocytes, there were numbers of cells with eosinophilic granulations.

In these four cases there were numbers of eosinophiles in gastro-intestinal lesions, and in only one case (Case XIV) were those cells found in other organs. In the case of chronic dysentery they were numerous in the very much thickened splenic pulp. In con-

nection with Case XXI it is interesting to note that in a case of
chronic salpingitis and ovarian abscess, occurring in a woman with
tapeworm, eosinophiles were present in great numbers in the in-
flammatory lesions and in the blood-vessels. Unfortunately a dif-
ferential count of the leucocytes of the blood was not made.

*Case XXII.* Female, aged 65 years. Carcinoma of bladder
and uterus with numerous eosinophiles in the stroma of the tumor;
interstitial splenitis with polymorphonuclear eosinophiles in the
pulp. A few polymorphonuclear eosinophiles were scattered
through the splenic pulp. Sections made from various portions
of the uterine tumor showed typical adeno-carcinoma with large
alveoli.

In the scanty stroma and in the surrounding tissues there were
large numbers of mononuclear and polymorphonuclear cells with
eosinophilic granulations. These cells were especially numerous
in the media of small arteries, where they lay between the muscle
cells and were often much elongated.

The following case is of special interest as being the first case
of chronic interstitial nephritis in the round cell infiltration of
which we have been able to find cells with eosinophilic granula-
tions; it showed transition forms between the plasma cell and the
eosinophile cell.

*Case XXIII.* Female, aged 44 years. Chronic interstitial
nephritis and splenitis with eosinophilic mono- and polymorphonu-
clear cells in the kidneys. Sections of the kidneys showed wide-
spread interstitial nephritis with marked atrophy of the renal tis-
sue, both tubular and glomerular, with fibroid interstitial growth.
Among the cells in the areas of round cell-infiltration there were
some large mononuclear cells with non-granular cytoplasm which
stained deeply and diffusely with eosin. Besides these there were
many cells with granular cytoplasm which stained deeply with
eosin. The liver and spleen showed nothing of special interest.

The next case is an instance of acute suppurative nephritis en-
grafted on chronic arteriosclerotic nephritis. The exudation in
this case was marked by the presence of large numbers of poly-
morphonuclear eosinophiles in association with plasma cells and
polymorphonuclear neutrophiles.

*Case XXIV.* Male, aged 62 years. Haemorrhagic cystitis,
abscess of prostate, pyelo-nephritis; chronic interstitial nephritis;

polymorphonuclear neutrophilic and eosinophilic leucocytes and plasma cells in the exudation.

Sections of the kidneys showed much the same changes. There was well-marked arteriosclerotic nephritis with atrophied hyaline and fibrous glomeruli, tubular atrophy and fibrous vessel increase. Scattered through the sections there were larger and smaller areas of abscess formation with diffuse infiltration with great areas of plasma cells and polymorphonuclear neutrophilic and eosinophilic leucocytes. The most numerous cells were the neutrophiles. The capillaries were dilated, the tubules were disorganized, and the epithelial cells were in various stages of degeneration. In the deep cortical and medullary portions there were larger and smaller areas of diffuse infiltration with plasma cells, polymorphonuclear neutrophiles and eosinophiles. These cells were seen both within and without the tubules, some tubules being enormously distended with them. Cocci, short, thin bacilli, and long and stout bacilli were found. The long thick bacilli were present in great numbers. No eosinophilic cells were found in sections of the bladder and prostate.

In the next three cases* eosinophilic cells were found in acute interstitial nephritis.

*Case XXV.* Male, aged 57 years. Acute and chronic interstitial nephritis with the presence of mono- and polymorphonuclear eosinophiles and plasma cells in the interstitial tissue, epithelioma of the bladder.

Cultures were negative. Urotropin had been administered several days before death. Sections of the kidneys showed thickening of the capsules, with thinning of the cortices, which were the seat of widespread interstitial nephritis. Most of the glomeruli had disappeared, and of those which were left some were markedly thickened, while others were hyaline. The tubules were extensively atrophied, and there was a diffuse growth of fibrous tissue, rich in cells, most of which were polymorphonuclear neutrophiles, though a number of eosinophiles were seen among them. Larger and smaller collections of eosinophiles were present in the tissue. The blood-vessels were dilated, and many of the capil-

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* These three cases were reported in full in the American Journal of the Medical Sciences, December, 1900.

laries and small veins contained numbers of leucocytes. In many places the process was acute rather than chronic, the tissues being filled with leucocytes. A few small scattered abscesses were seen in the tissue. The medullary portion showed marked congestion, the tissue was compressed and atrophied, and here and there larger and smaller collections of small round cells were seen. In the adventitia of many of the small arteries there was marked cellular infiltration. These cells were for the most part small round cells and plasma cells, but a number of large mononuclear and smaller polymorphonuclear eosinophilic cells were seen. In the adventitia of one of the small arteries, near some typical plasma cells, and some large mononuclear cells, two very interesting cells were seen. One was the size of a large mononuclear leucocyte, which had a distinct kidney-shaped nucleus. The cell had the appearance of a typical transition cell of the blood. Next to it was a cell slightly smaller in size, which was crowded with rather fine granulations, much smaller than those of a typical eosinophile; these granulations stained very deeply with eosin. The nucleus of this cell was slightly oval, and marked by larger and smaller deeply staining chromatic masses. This cell was apparently a transition of a large mononuclear into an eosinophilic leucocyte. Large numbers of eosinophiles were scattered through the kidney and in the areas of round cell infiltration.

*Case XXVI.* Female, aged 30 years. Acute interstitial nephritis with mono- and polymorphonuclear eosinophilic leucocytes and plasma cells in the intertubular exudation. Tuberculosis of bronchial glands with eosinophiles in the tuberculous tissue. Prolapsus uteri, abortion, vaginal hysterectomy. Small stitch abscess containing *Staphylococcus aureus.* In the bronchial glands there were a number of areas containing giant and epithelioid cells, while in the lymph spaces and stroma there were numerous mono- and polymorphonuclear eosinophiles.

In the kidneys there were numerous areas of cellular infiltration, in many of which the glomerular capillaries were thick and congested and showed an increase of cells, some of which had eosinophilic granulations. The tubules were compressed by an accumulation of cells in the intertubular tissue. These cells were for the most part plasma cells, but a considerable number of eosinophiles were present. The latter were seen in the capillaries as

well as in the tissues. The epithelial cells of the tubules were compressed and many were swollen and granular.

*Case XXVII.* Female, aged 35 years. Acute interstitial nephritis with numbers of eosinophiles and plasma cells in the exudation.

*Anatomical Diagnosis.*—Streptococcus septicaemia following abortion; stomatitis, pharyngitis, bronchitis, bronchopneumonia, and oedema and congestion of the lungs; acute interstitial nephritis, acute splenic tumor, retained placenta. The kidneys were large; the right weighed 370 and the left 330 grammes. The capsules stripped off readily, the surfaces were smooth, pale and stained with bile pigment. On section the organs were hyperaemic and markedly oedematous and opaque. The consistency was increased. The cortices averaged 1 cm. in thickness; the glomeruli were inconspicuous; both organs were bile stained. On microscopic examination the kidneys showed marked oedema and congestion. The glomerular capillaries were dilated and contained a few polymorphonuclear eosinophiles. The capsular epithelium was swollen and granular as was the epithelium of the convoluted tubules. There were larger and smaller areas of cellular infiltration in the intertubular tissues of the cortex both near the surface and near the medulla. In many places the tubules were markedly compressed by this exudation, in which three main varieties of cells could be distinguished, viz., lymphocytes, plasma cells and polymorphonuclear cells with eosinophilic granulations. Some tubules were filled with desquamated epithelial cells and leucocytes in varying numbers. Throughout the kidneys the bloodvessels, especially the capillaries, contained large numbers of polymorphonuclear eosinophilic cells, which were most numerous near the areas of cellular infiltration. In these areas of interstitial nephritis the most numerous cells were plasma cells; next in number to these ranked the eosinophilic cells. In some places the eosinophilic cells were the most numerous cells in the exudation.

There were five cases of nephritis with eosinophiles in the renal lesions. The first (Case XXIII) was a typical case of chronic interstitial nephritis, in the cellular infiltration of which eosinophiles were found. In Case XXIV, the kidneys were the seat of a moderate degree of arteriosclerotic nephritis, and there was a double-sided acute suppurative nephritis, secondary to abscess of

the prostate, in the exudation of which besides polymorphonuclear neutrophiles there were many plasma cells and eosinophiles. Case XXV was also an example of moderate chronic nephritis with acute suppurative nephritis, secondary to chronic cystitis and epithelioma of the bladder. The eosinophiles and plasma cells were very numerous. In Cases XXVI and XXVII, there was typical acute interstitial nephritis with large numbers of eosinophiles and plasma cells in the exudation. In both cases there had been abortion and in the last case streptococcus septicaemia. The eosinophiles were so numerous that the process might with propriety be called acute eosinophilous nephritis.

*Case XXVIII.* Male, aged 19 years. Caseous and miliary tuberculosis with oedema of the lymph glands with the presence of large numbers of eosinophiles. Recent tubercular pleurisy and pericarditis. General infection with *Staphylococcus aureus.*

Sections of various lymph glands showed marked oedema with miliary and caseous tuberculosis. Sections of one mesenteric gland showed as follows:

Larger and smaller areas of caseation were surrounded by a reticular fibrous tissue in the meshes of which there were many cells, among which there were giant cells, epithelioid cells, plasma cells and lymphocytes. There was enormous oedema which distended the spaces of the reticular tissue as well as the lymph channels. Many of the lymph channels, especially in the centre of the gland, were crowded with cells, most of which were plasma cells, hyaline leucocytes and lymphocytes, with relatively few polymorphous nuclear cells. In many plasma cells nuclear figures were seen. In the widely distended reticulum, there were relatively few cells, most of which were very large oval cells, some with densely staining and some with vesicular nuclei, surrounded by a large amount of finely granular protoplasm. The nuclei were often eccentric and sometimes reniform. The granules were not eosinophilic, but the cells were markedly phagocytic, and often contained plasma cells, lymphocytes and even eosinophiles. The germinal centres were increased in size, the most numerous cell being the plasma cell. There were also many eosinophiles. Nearly everywhere in the tissue there were variable and often large numbers of coarsely granular eosinophiles, some with polymorphous nuclei but most with a single, rather deeply-staining nucleus.

Many cells with nuclei similar to those of plasma cells surrounded with fine eosinophilic granulations were seen. The blood-vessels were not congested and showed no increase of leucocytes.

*Case XXIX.* Male, aged 17 years. General miliary tuberculosis with mono- and polymorphonuclear eosinophiles in the mesenteric and retroperitoneal lymph glands, which were large, soft and oedematous.

Sections from these glands showed typical miliary and conglomerate tubercles containing many giant cells and often showing caseation. In many places there was marked oedema, increase of the cells of the germinal centres and dilatation of the lymph channels, with the presence of large numbers of cells in the stroma and in the channels. These cells were chiefly plasma cells but there were also present a number of mononuclear eosinophiles with eccentric nuclei, closely resembling plasma cells in all respects except eosinophilic granulations. A few ordinary polymorphonuclear eosinophiles were also present.

These two cases are of great interest, for with the eight cases of tuberculosis with eosinophilic infiltration met with in our operative material, and the lymph gland tuberculosis of Case XXVI and the lung tuberculosis in Case XVII, they make twelve instances in which we have observed eosinophiles in tubercular lesions. The development of eosinophiles from plasma cells and hyaline leucocytes could be readily traced in the tuberculous lymph glands.

*Case XXX.* Male, aged 49 years. Eosinophiles in a wall of a liver abscess secondary to pneumonia and empyaema. General streptococcus infection. Sections of the wall of the hepatic abscess showed marked congestion of the blood-vessels with compression of the liver cells. The abscess wall was infiltrated with polymorphonuclear neutrophiles, plasma cells and coarsely granular eosinophiles.

This is the third case in which we have found eosinophiles in the liver. Case XIV showed them in the portal spaces in a child dead of burns; while in Case XV they were found in the vessels of angioma of the liver of a woman with pelvic abscess.

*Case XXXI.* This case has already been published by one of us (Howard).[4] For the clinical history and autopsy we are in-

[4] Howard, W. T., Jr. Philadelphia Medical Journal, 1899, vol. IV, p. 1085.

debted to the kindness of Dr. Hoover. Female, aged 35 years, was ill for three weeks with diarrhoea and vomiting and complained of pain in the abdomen and the muscles of the extremities. Coverslip preparations of the blood stained with Ehrlich's triacid stain, on examination by Dr. Hoover, showed a slight leucocytosis, without however an increase in the number of eosinophiles. Although Dr. Hoover did not make a differential count, he is confident that there was no circulatory eosinophilia. A piece of the extensor quadratus of this case was excised and showed large numbers of *Trichina spiralis.* Death occurred at the end of three weeks from the onset.

*Anatomical Diagnosis.*—General infection of the voluntary muscles with *Trichina spiralis;* acute yellow atrophy of the liver; infarction of the spleen; fatty degeneration of the heart and kidneys; congestion of the lungs and intestines.

Cultures and coverslip preparations made from the various organs showed no bacteria. Teased preparations of the tongue, the diaphragm, quadratus lumborum, psoas, and quadriceps femoris muscles showed large numbers of actively motile trichinae. No trichinae were found in the intestinal contents.

Sections of the heart showed congestion of the capillaries and small veins—in some of the latter there were small accumulations of large and small mononuclear leucocytes; no cells with eosinophilic granulations were found. Larger and smaller areas of cellular infiltration were seen between some of the muscle fibres, the cells consisting of lymphocytes, plasma cells, a few polymorphonuclear neutrophilic leucocytes, and a number of both polymorpho- and mononuclear cells with marked eosinophilic granulations.

In the lungs there was found marked oedema with congestion. In the peribronchial tissue and in the lymph spaces, but never in the small blood-vessels a few polymorpho- and mononuclear eosinophiles were found. The larger pulmonary veins, however, contained numbers of these cells.

In sections of the liver, it was often impossible to recognize the tissue. There was widespread fatty degeneration and nuclear fragmentation. In some places the liver cells were small, shrunken, very granular, and stained intensely with eosin; in other places they were swollen, and contained large and small fat drops. The

blood-vessels showed no special changes, but many capillaries contained numerous neutrophiles, but no eosinophiles.

The spleen showed congestion, with thickening of capsule, trabeculae and pulp, the latter containing many polymorphonuclear eosinophiles. The kidneys showed congestion and oedema, with cloudy swelling of the epithelium of the convoluted tubules.

In the stomach and large and small intestines there were a number of polymorpho- and mononuclear eosinophiles in the interglandular stroma.

In sections of the tongue and diaphragm there were large numbers of trichinae of varying size situated in the muscle fibres. The trichinae were usually single, but in many places two and even three were seen in the same cyst. The trichinae were situated in the muscle fibres, and were surrounded by a hyaline capsule of varying thickness. In many places, especially at the poles of the cysts, there was very active multiplication of muscle nuclei, which were for the most part long, vesicular, and often irregularly constricted. Muscle fibres containing trichinae, both near to and at a distance from the latter were swollen, had lost their striations and showed large and small finely granular amorphous areas of degeneration which stained deeply with eosin. About some trichinae there was little cellular reaction, while about others great numbers of cells were seen. In many places there was marked proliferation of muscle nuclei in fibres in which no trichinae were to be found.

The process was evidently an acute one. There was no evidence of calcification. In the cellular reaction about the trichinous areas the following varieties of cells could be distinguished:

I. Cells in every way like plasma cells, having a single, round, or oval, somewhat pale nucleus, containing larger and smaller chromatin masses, surrounded by a varying amount of homogeneous cytoplasm which stained faintly with eosin. In some of these cells the nucleus was centrally placed, but in most it was eccentric. In shape these cells were round or long oval; occasionally they were very much elongated (amoeboid movement?). They were the most numerous cells present.

II. Cells with nuclei of the same size and appearance as No. I, surrounded by homogeneous cytoplasm which stained deeply with eosin. These cells were fairly numerous.

III. Cells with nuclei similar to Nos. I and II, surrounded by cytoplasm containing very fine eosinophilic granulations.

IV. Cells of the size of large mononuclear leucocytes, with rather deeply staining nuclei, surrounded by either finely granular or coarsely granular deeply staining eosinophilic granulations. These cells were quite numerous.

V. Polymorphonuclear cells, with reniform horseshoe-shaped, or trilobate nuclei, and cytoplasm containing either finely or trilobate nuclei, and cytoplasm containing either finely or coarsely granular eosinophilic granulations. These cells were numerous, and were the exact counterpart of the polymorphonuclear eosinophilic cell of the blood.

VI. A variable number of small round cells with single deeply-staining nuclei, surrounded by a narrow rim of granular protoplasm. These were typical lymphocytes.

VII. Cells of varying size, usually very large, containing large, elongated, vesicular nuclei. These cells were very numerous in places, and were evidently proliferating muscle cells.

VIII. A few typical fibro-blasts.

IX. A few giant cells with from four to six nuclei, and homogeneous non-granular protoplasm.

X. A few neutrophilic polymorphonuclear leucocytes.

In some places, especially at the margins of the areas of cellular infiltration, there were seen rows of polymorpho- and mononuclear cells with eccentric nuclei, and many with fine or coarse eosinophilic granulations.

The blood-vessels were dilated but showed no increase of leucocytes in the small veins, but in some capillaries there were a considerable number of mononuclear cells.

Careful search failed to discover transition of polymorphonuclear neutrophilic cells into eosinophiles. There was absolutely no evidence of this mode of origin for the eosinophilic cells.

The most numerous and apparently the most important cell in the reaction in this case was the plasma cell. The cells with eosinophilic granulations were much less numerous than the plasma cells. The development of the former from the latter could be readily and easily traced as follows: The homogeneous protoplasm of the plasma cell becomes first faintly and then strongly eosinophilic. In the next stage, fine, and later coarser eosino-

philic granulations develop, producing typical mononuclear eosino-
philes. Some of these latter develop polymorphous nuclei. With
the development of granulations the plasma cells often increase in
size. The size of the eosinophilic cells varies, however, within
rather wide limits. In this case at least, it seems certain that the
eosinophiles were formed in the areas of cellular reaction about
the muscle trichinae, and were not brought there from a distance
by the blood-vessels being drawn by chemotactic substances thrown
out by the parasites, or furnished by the degenerating muscle.
The substances present, whatever their nature, exerted a chemo-
tactic action on the plasma cells.

The presence of increased numbers of eosinophiles in the stroma
of the mucosa of the stomach and intestine is probably to be ex-
plained by the recent presence of trichinae in the intestine and
intestinal wall. Here too the eosinophiles probably had their
origin in plasma cells. The course of the disease in this case was
more acute than in the cases of Brown,[5] Gwyn,[6] Atkinson[7] and
Stump[8] and this fact probably explains the absence of circulatory
eosinophilia. Had the individual lived longer, or the infection
been less severe, it is probable that eosinophiles would have made
their way into the blood. It is recognized that the presence of
a circulatory eosinophilia during life cannot be positively denied
in the absence of a differential count, on the strength of Dr.
Hoover's impression from the examination of stained preparations.
If, however, the eosinophiles were much increased in the circula-
ting blood during life, it would be strange to find the percentage
normal in differential counts of preparations made from the blood
of the organs after they reached the laboratory.

This case demonstrates among other things that trichinosis may
exist and run a fatal course apparently without increase of eosino-
philes in the circulating blood, and that a high grade of eosino-
philia, such as was present in the cases of Brown, Gwyn, Atkinson
and Stump (42, 49, 68.2, 72, 58.5 and 52 per cent) speaks for a

[5] Brown, T. R.   Bulletin of the Johns Hopkins Hospital, 1887, vol. VIII.
Journal of Experimental Medicine, 1898.

[6] Gwyn, N. B.   Centralbl. f. Bakteriologie, 1899, Band xxv, S. 746.

[7] Atkinson.   Philadelphia Medical Journal, June 3, 1899.

[8] Stump.   Philadelphia Medical Journal, June 17, 1899.

good prognosis and indicates that the organism is reacting well to the poison of the trichinae. The marked degeneration of the liver and kidneys of our case shows that the tissues were acted upon by a powerful poison. Brown's observation that the eosinophiles in the muscle in trichinosis are formed in the lesions and are not attracted there by chemotactic substances, is supported by the findings in this case. We believe that trichinae or a poison or poisons secreted by them have a positive chemotaxis for hyaline leucocytes, plasma cells, and polymorphonuclear leucocytes and that for some unknown reason certain of the first two varieties of cells develop eosinophilic granulations.

### HISTOGENESIS OF EOSINOPHILIC CELLS.

There are several theories in regard to the histogenesis of eosinophilic cells and in support of each theory a certain amount of evidence has been brought forward. These theories and their main supporters are as follows:

I. From polymorphonuclear neutrophilic leucocytes by a kind of ripening process, Max Schultze,[9] Gulland,[10] Zappert,[11] Brown[12] and others.

II. From eosinophilic myelocytes in the bone-marrow only, Ehrlich.[13]

III. Division of pre-existing cells of the same kind, by mitosis, Müller und Rieder,[14] and Van der Stricht;[15] by amitosis, Rénaut,[16] Denys[17] and Arnold; Gulland,[18] who has exhaustively studied the leucocytes of many species of animals thinks that all forms of leucocytes give rise on division to lymphocytes, but that occasionally on the division of eosinophiles the daughter-cells may contain a few eosinophilic granulations.

[9] Schultze, Max. Arch. f. Mikroskop. Anat. 1865, I.
[10] Gulland. Journal of Physiology, 1895–6, Vol. xix.
[11] Zappert. Zeitschrift f. Klin. Med. 1893, Bd. xxiii.
[12] Brown. Loc. cit.
[13] Ehrlich and Lazarus. Die Anemie. Wien, 1898.
[14] Müller und Rieder. Deutsch. Arch. f. Klin. Med., 1891–2, Vol. xlviii.
[15] Van der Stricht. Quoted by Brown, loc. cit.
[16] Rénaut. Quoted by Brown, loc. cit.
[17] Denys. Quoted by Brown, loc. cit.
[18] Gulland. Loc. cit.

IV. From the connective-tissue of various parts of the body, Gollasch,[19] Neusser,[20] Weiss[21] and others. Kanthack and Hardy[22] found these cells in numbers in the caelomic cavity and connective-tissues of animals.

V. Occurring as incompletely developed erythrocytes, derived from haematoblasts, Przewaski.[23]

VI. From the engulfing of haemoglobin of haematoblasts by leucocytes, Sacharoff,[24] who thinks that the granules are connected with the dispersion of haematin and that the intense coloration of eosinophilic granulations is due to the greater thickness of their iron-bearing paranuclein. According to Sacharoff, bacteria taken up by leucocytes may furnish eosinophilic material, their nuclein being changed into eosinophilic paranuclein. Klein[25] thinks that eosinophiles are formed from other leucocytes by the taking up of iron derived from red blood cells.

VII. From lymphocytes by transition, Pappenheim.[26]

It is neither impossible nor indeed improbable that these cells may have their origin in any of these several ways.

Ehrlich and Lazarus strongly combat the idea of the local formation of eosinophiles.

While not denying that these cells may have their origin in many ways, in the study of our rather large material, we have never been able to trace any one of these modes of origin (except from eosinophilic myelocytes). We have been struck on the other hand with the great frequency with which the origin of these cells can be traced from the hyaline leucocyte, and especially from the plasma cell. In case after case, in organ after organ, and especially in the lymphoid tissues (the thymus, lymph glands, the spleen, and the bone-marrow), in the gastro-intestinal mucosa (gastritis, lympho-sarcoma, colitis, and appendicitis), in

[19] Gollasch. Fortschritte d. Med., 1899, Bd. vii.

[20] Neusser. Wien. klin. Wochenschr., 1892, Bd. xii, p. 64.

[21] Weiss. Quoted by Brown, also by H. F. Müller. Centralbl. f. allgem. Path. u. path. Anatomie.

[22] Kanthack and Hardy. Journal of Physiology, 1894–5, Vol. xvii.

[23] Przewaski. Centralbl. f. allg. Path. und path. Anat., 1896, Bd. vii, S. 177.

[24] Sacharoff. Centralbl. f. Bakteriologie, 1897, Bd. xxi, S. 265.

[25] Klein, S. Centralbl. f. Innere Med., 1899, Bd. L, S. 28.

[26] Pappenheim. Virchow's Archiv., 1899, Bd. 157, p. 71.

exudations rich in lymphocytes, hyaline leucocytes and plasma cells (acute and chronic nephritis, salpingitis and ovarian abscess, etc.) and in various other processes, we have observed the transition of both these varieties of cells into eosinophiles.

As already pointed out, the hyaline, or better as Kanthack and Hardy aptly term it, the "ground glass" cytoplasm of the hyaline cell or the plasma cell (for the latter often comes from the former) stains more deeply with eosin than its neighbors. In other cells with clear nuclei, which are often eccentric, there are fine granules which stain deeply with eosin. Other cells with similar nuclei have more coarsely granular and others still very coarsely granular cytoplasm. With the development of the eosinophilic granules the cells usually, but by no means always, increase in size. With the development of the granules the nuclei become less vesicular, and the nuclear chromatin more diffuse. Many coarsely granular as well as finely granular mononuclear eosinophiles were seen, but always a large proportion of the mononuclear cells develop polymorphous nuclei. We have been struck with the large proportion of mononuclear eosinophiles present in some cases. If the idea of Gulland and others that the change in the shape of the nucleus of the leucocyte is dependent largely upon the motion of the cell is correct, the above fact is another argument in favor of the origin of eosinophiles from plasma cells. In size the eosinophile in the tissues varies within rather wide limits, from the size of a small plasma cell, scarcely larger than a lymphocyte, to that of the typical eosinophile of the blood.[27]

In Case XX we observed appearances which we cannot interpret otherwise than that they represent the development of coarsely granular eosinophiles from smooth muscle cells. In the same case there were also many examples of the plasma cell origin of these cells.

### CHARACTER OF EOSINOPHILIC GRANULATIONS.

We have nothing to add to the knowledge of the character and composition of these granules. For the literature of the subject

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[27] A good description with a full account of the plasma cell will be found in Councilman's article on Acute Interstitial Nephritis, Journal of Experimental Medicine, 1898, vol. III, p. 393. See also Marschalko's Zur Plasmazellenfrage, Centralbl. f. Allgem. Pathologie und path. Anatomie. 1899, Bd. x, S. 851.

the reader is referred to Brown's recent article in the Journal of Experimental Medicine (loc. cit.).

First mistaken for fat, which was disproved by Ehrlich,[28] who first suggested that they represented a nutritive reserve formed by the cell, these granules have been considered in turn non-proteid (Schwarze);[29] proteid (Zappert);[30] haemoglobin or its derivatives (Przewaski[31] and others); nucleo-albumin (Sherrington);[32] and secretory granules of a defensive nature (Hankin),[33] Kanthack and Hardy.[34] Gulland,[35] however, insists that they are not products of the metabolic activity of the cell imbedded in the protoplasm, but that they represent an altered condition of the microsomes, form a part of the cytomitoma, and are therefore, plastic and not paraplastic, as is generally believed. Gulland thinks that they are concerned in the amoeboid activity of the cell. As previously stated we were unable to demonstrate the presence of iron in the granules of eosinophiles in hardened tissues.

## PRESENCE OF EOSINOPHILES IN NORMAL ORGANS.

Beside the blood, coarsely granular eosinophiles are normally found in various tissues of the human body, the spleen, thymus (earliest mention probably by J. Schaffer[36]), the lymph glands, bone-marrow, the gastro-intestinal tract (especially the stroma of the mucosa), in the kidneys and liver, and in various connective tissues. They are found in the same locations in various lower animals. They form from 25 to 40 per cent of the wandering cells in the peritoneal cavity in the guinea-pig, and from 30 to 50 per cent in rabbits (Kanthack and Hardy). In these animals they are also numerous in the subcutaneous tissue. We have found these cells but rarely in apparently normal organs of adults—in

[28] Ehrlich.   Loc. cit. S. 86, and in other writings.

[29] Schwarze.   Ueber eosinophile Zellen.   Inaug. Diss. Berlin, 1880.

[30] Zappert.   Loc. cit.

[31] Przewaski.   Loc. cit.

[32] Sherrington.   Proceed. Royal. Soc. Lond., 1894, vol. lv.   Also quoted by Brown.

[33] Hankin.   Centralbl. f. Bakteriologie, 1892, Bd. xi.

[34] Kanthack and Hardy.   Loc. cit.

[35] Gulland.   Loc. cit.

[36] Schaffer J.   Centralbl. f. d. Med. Wissensch., 1891, nos. 22 u. 23.

ten cases in the appendix, once in the Fallopian tube, and once in the gastro-intestinal mucosa."  Heidenhain found them constantly present in the intestinal mucosa of dogs, in which their numbers were greatly increased after fasting and a dose of magnesium sulphate.  Eosinophiles were not uncommonly found in various organs in children dying both with and without septicaemia.  We have also been able to confirm the observations of those who have described eosinophiles in numbers in the blood and tissues of the foetus.

## PRESENCE OF EOSINOPHILES IN INFLAMMATORY AND OTHER LESIONS.

With a few notable exceptions coarsely granular eosinophiles have not been described in inflammatory reactions and in infectious granulomata.  They have been found in gonorrhoeal pus in numbers by Gollasch[38] and others, in the sputum in bronchial asthma by Gollasch,[39] Leyden[40] and others, in the sputum in bronchitis by Leyden,[41] Teichmüller, Grünwald[42] and others; in the skin in lymphoderma perniciosa by Weiss[43] and in leprosy by Jadassohn;[44] in the blisters of pemphigus by Neusser[45] and others; in Dühring's disease by Leredde and Perrin;[46] in blisters produced artificially by Bettman[47] and by Kanthack and Hardy; in hemorrhagic pleurisy by Klein[48] and Harmasen.[49]  Gronven[50] found

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[37] On further study we find eosinophiles constantly present in the stroma of the mucosa and often in the lymphoid tissue of both the normal and inflamed appendix.

[38] Gollasch.  Loc. cit.

[39] Gollasch.  Loc. cit.

[40] Leyden.  Deutsch. Med. Wochenschr., 1891, Bd. xvii, S. 1085.

[41] Leyden.  Loc. cit.

[42] Grünwald.  Virchow's Archiv. 1899.  Bd. 158, S. 289.

[43] Weiss, Jul.  Jahrb. f. Kinderheilkunde, N. F. Bd. 35, quoted by H. F. Müller, Centralbl. f. allg. Path. u. path. Anat., 1893, Bd. iv, S. 539.

[44] Jadassohn.  Verhandl. d. deutsch. dermat.  Gesellsch. ii u. iii, quoted by H. F. Müller, loc. cit.

[45] Neusser.  Wiener Med. Wochenschr., 1892, 5 Jahr., S. 41.

[46] Leredde und Perrin.  Ann. de dermat. et Syph., iii ser. Tome vi, p. 281.

[47] Bettman.  Münchener Med. Wochenschr., 1898, no. 39.

[48] Klein.  Loc. cit.

[49] Harmasen.  Quoted by Klein.

[50] Gronven.  Inaug. Dissertation, Bonn, 1895.

eosinophiles in the false membrane of diphtheria in two cases, in pneumonia in diphtheria in one case, in a tumor of the larynx and in the bronchial glands in two cases. Przewaski [51] found large numbers of eosinophiles in carcinoma of the cervix uteri in four cases, while Fledbausch [52] observed them in variable numbers in epitheliomata, carcinomata and lymphosarcomata. They were most numerous about inflammatory and necrotic areas. Grünwald [53] observed coarsely granular eosinophiles in the sputum in one case each of asthma, fetid bronchitis and phthisis and in four nasal polyps. They were absent in pneumonia, pleurisy, pericarditis, gonorrhoea, abscess of the breast and the ear and in chancre. Grünwald describes cells with fine, scattered granules which are eosinophilic to a lesser degree than those of the ordinary eosinophiles, and to these cells which he found in numbers in sputum and other discharges he gives the name "hypoeosinophiles." T. R. Brown [54] and one of us (Howard [55]) found large numbers of eosinophiles in the reaction about trichinae in human muscle. In our material derived from operation eosinophiles occurred in 13.09 per cent of the cases, of which over 74 per cent were inflammatory, and including the cases of syphilis and tuberculosis 83.8 per cent were infectious processes.

To recapitulate: we have found both mono- and polymorphonuclear eosinophiles in the gastro-intestinal tract, the spleen, thymus, appendix and Fallopian tubes in apparently normal organs and in the following pathological conditions: abscess of Bartholin's gland, angioma of the liver, appendicitis, in carcinomata of the arm, the bladder, and of the uterus and scrotum, in corpus luteum cysts, in chronic cystitis, in dysentery, in endometritis, in epithelioma of the vagina, face, and of lymph glands, in atrophic gastritis and arsenical gastritis, in interstitial splenitis, in gonorrhoeal lymphadenitis, in lymphosarcoma, in nasal polyps, in acute and chronic interstitial nephritis, in suppurative nephritis, in omentitis, in pelvic abscesses and in a pilonidal abscess, in oophoritis and peri-

[51] Przewaski. Loc. cit.
[52] Fledbausch. Virchow's Archiv. 1900. Bd. 161.
[53] Grünwald. Loc. cit.
[54] Brown, T. R. Loc. cit.
[55] Howard. Loc. cit.

oophoritis, in lobar pneumonia, in proctitis, in acute and chronic salpingitis, in trichinosis, in the spleen in malaria, and in tuberculosis of the muscles, of the skin and of the lungs, bone, ureter and lymph glands, and in syphilis of the skin.

We have failed after careful search to find them in organizing blood-clots, haemorrhages into tissue, haemorrhagic infarcts, organizing thrombi of the heart and blood-vessels, organizing corpora lutea, and a number of cases of abortion remnants containing blood.

### Modes of Development and Causes of Increase in the Number of Eosinophiles in the Blood.

In the light of our present knowledge, it is clear that these occur in at least two ways: (a) When an abnormally large number of eosinophiles are needed in a particular part of the body, i. e., when substances possessing positive chemotaxis for these cells are present in a part they are drawn from the haematopoietic organs, and reach the part by means of the lymph and blood channels; thus appearing in the blood in increased numbers. (b) When under proper stimulation, numbers of eosinophiles have been formed in a part, and after the need for them is past, and for other reasons not yet understood, they make their way into the lymph and blood-vessels, producing eosinophilia.

A third explanation, one for which, however, there does not seem to be any positive evidence, is that circulatory eosiniphilia may develop by the transition of certain forms of leucocytes into eosinophiles in the circulating blood. A priori, there is no reason against this mode of origin. If these cells develop from other leucocytes (hyaline cells, plasma cells, lymphocytes, and polymorphonuclear neutrophiles) in the tissues, why not in the blood as well?

In our cases (consult Groups II and III), especially the inflammatory cases, two sources for the eosinophiles in the lesions were demonstrated, i. e., the blood-vessels, and transition from plasma cells and hyaline leucocytes in the lesions. In many cases the two processes could be traced in the same lesion.

Kanthack and Hardy[46] have shown that these cells are the first

[46] Kanthack and Hardy. Loc. cit.

to wander into capillary tubes, and into Ziegler's plates containing bacteria and other irritants in the peritoneal cavity and subcutaneous tissues of rabbits and other animals. They also showed that these cells are formed or accumulate very rapidly in the connective-tissues of animals after injury. We found the eosinophiles the most numerous cells present in multiple renal abscesses occurring in a rabbit after inoculation with *Staphylococcus aureus.* T. R. Brown and Klein are among the authors who have brought out the fact that eosinophiles are formed in the lesions. Klein thinks that polymorphonuclear neutrophilic leucocytes attracted to a place and left to their fate become eosinophiles.

Leredde[57] believes that the pemphigus foliaceus is due to the excretion of eosinophiles by the skin, and concludes that the skin affection is a secondary matter. He regards the affection as essentially one of the blood due to the reaction of the haematopoietic organs, especially the bone-marrow, under the influence of multiple intoxications. This conception is quite the opposite of Neusser's view. It is difficult to conceive of the *excretion* of eosinophiles by the skin. It is much more in accordance with our knowledge to think that these cells are attracted to the foci of disease, the haematopoietic organs being stimulated to their production, or that they were formed in the lesions.

Our own conception is that in many conditions the formation of eosinophiles in the regular haematopoietic centres is stimulated by a variety of substances, many of which also have the property of attracting these cells. In other conditions other forms of leucocytes, but especially hyaline leucocytes and plasma cells and possibly certain tissue cells, develop eosinophilic granulations in various lesions. We have evidence that these two processes may occur together in the same case.

Why are eosinophiles attracted to or formed in inflamed areas and in other lesions?

Müller[58] thinks it will be found that both asthma and pemphigus are caused by substances (bacterial?) which have a positive chemotaxis for eosinophiles, while Neusser[59] believes that eosino-

[57] Leredde.   Ann. de dermat. et Syph. III n. ser. Tome x, p. 355.
[58] Müller, H. F.   Loc cit.
[59] Neusser.   Loc. cit

philes may be derived from the tissue cells on stimulation of the sympathetic nerves, in the same way that granules are secreted in the mucous cells of the salivary glands of the dog after stimulation of the sympathetic nerve of the gland. According to this view the bronchial mucous membranes in asthma and the skin in pemphigus, play the part of blood-forming organs in secreting eosinophilic granulations.

Goldman,[60] Jadassohn,[61] H. F. Müller,[62] hold that there are certain substances which possess a positive chemotaxis for eosinophiles. Ehrlich and Lazarus,[63] adopting this view, state that this property is possessed chiefly by the products of the degeneration of epithelial and epithelioid cells. In this way they explain the common occurrence of eosinophilia in skin diseases, in atrophic lesions of the gastric, intestinal and bronchial mucous membranes, in the neighborhood of carcinoma and in lupus after tuberculin injection. They think that the mucin or mucin-like bodies in mucous polyps of the nares, must attract these cells.

For most forms of eosinophilia the direct cause, according to these authors, is to be sought for in tissue destruction and its products. They also suggest that the eosinophilia of the various forms of helminthiasis is due to the positive chemotaxis exerted on these cells by poison secreted by the parasites.

As we have already stated, Kanthack and Hardy observed that various substances, including silver nitrate, turpentine, and copper, *B. ramosus, B. cholerae, B. pyocyaneus,* and *B. anthracis* in animals and liquor epipoeticus upon the human arm, all possessed a strong chemotaxis for eosinophiles. In our operative material bacteriological examinations were negative in many cases, especially in salpingitis and ovarian abscess. In some of these cases a more or less clear history of gonorrhoea was obtained. Taking the operative and autopsy material together, the following varieties of bacteria were found in processes marked by the presence of eosinophiles: *Streptococcus pyogenes, Staphylococcus pyogenes aureus* and *albus, Gonococcus, Pneumococcus, B. coli communis,*

[60] Goldman. Centralbl. f. allgem. Path. u. path. Anat. 1893, Bd. lll, S. 665.
[61] Jadassohn. Loc. cit.
[62] Müller, H. F. Loc. cit.
[63] Ehrlich u. Lazarus. Loc. cit. S. 113 and 114.

*B. mucosus capsulatus, B. aërogenes capsulatus* (once in the kidney), *B. tuberculosis.*   To these may be added the two cases of infection with animal parasites, malaria and trichinosis.

In the autopsy series the *Streptococcus* was the organism most frequently found.

That coarsely granular eosinophiles play an important part in many inflammatory, and a variety of other, processes, ·is shown by the cases reported in this article as well as by the experiences of other observers.   Our experience agrees with that of Metschnikoff [44] and Kanthack and Hardy who state that these cells never act as phagocytes.   We have never seen them near bacteria, but have found them in great numbers about trichinae, without, however, ever invading the cysts.

We have not been able to confirm the statement of Kanthack and Hardy, that these cells apply themselves to bacteria in exudations and use up their granules in fighting them.

<div align="center">

SUMMARY.

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In the routine examination of 825 specimens removed by operation, coarsely granular eosinophiles were found in the normal appendix in 10 cases, and in the normal Fallopian tube in one case.

These cells occurred in larger or smaller numbers in the tissues or blood-vessels, or both, in 108 cases, or in 13.09 per cent; 83.3 per cent of these lesions were infectious in origin.

In seven cases (one adult and the rest children), four of which died of infectious processes, eosinophiles were present in apparently normal organs.

In 120 consecutive autopsies 27 cases showed larger or smaller numbers of eosinophiles in various organs showing pathological changes.   In this series they occurred in the spleen in chronic interstitial splenitis in 11 cases, in the thymus in 5 cases, in lymph glands in 3 cases, in the stomach in 3 cases, in the intestine in 2 cases, in the kidney in 5 cases, in the lungs in 3 cases, in the liver in 3 cases, in the heart in 1 case, in the skeletal muscles in trichinosis in 1 case.

In some cases these cells were brought to the part by the blood-

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[44] Metschnikoff.   Pathologie comparée de l'Inflammation p. 186.
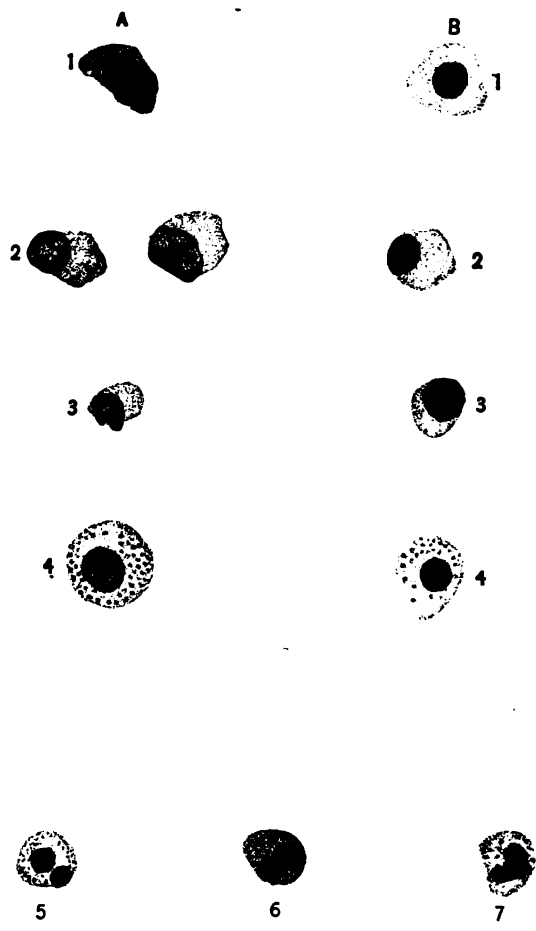
vessels, and in others they were formed in the lesions, while in still other cases their presence was to be accounted for in both of these ways.

In a large number of cases the development of coarsely granular eosinophiles was traced from plasma cells and in some cases from hyaline leucocytes.

### DESCRIPTION OF PLATE.

The sections from which the drawings were made were hardened in Zenker's fluid and stained with haematoxylin and eosin or with eosin and methylene blue. The figures were drawn with the aid of a Zeiss camera lucida with a Reichert 1–12 oil immersion lens and 4 ocular.

Figures A 2, 3 and 4 show the development of eosinophiles from the plasma cells; figures B 2, 3 and 4 show transitions between the hyaline leucocyte and the eosinophile; figures 5, 6 and 7 represent eosinophiles which may have had either of the above modes of origin.

A. 1. Typical plasma with clear nucleus eccentrically placed, cytoplasm unstained by eosin (basophilic).
2. Plasma cell the cytoplasm of which stains diffusely pink with eosin (acidophilic).
3. Plasma cell with eccentric nucleus and cytoplasm with fine eosinophilic granulations.
4. Large cell with a round nucleus similar to that of the plasma cell and with coarse eosinophilic granulations of its cytoplasm.

B. 1. Large mononuclear leucocyte with centrally placed deeply staining nucleus and hyaline faintly basophilic cytoplasm.
2. Large mononuclear leucocyte with deeply staining eccentrically placed nucleus and cytoplasm which stains diffusely pink with eosin (acidophilic).
3. Cell with nucleus similar to 2, but with numerous fine eosinophilic granulations of its cytoplasm.
4. Cell with round deeply staining nucleus and large scattered eosinophilic granulations of its cytoplasm.

Figures 5, 6 and 7 represent polymorphonuclear cells with varying numbers of coarse eosinophilic granulations and which apparently may have developed from either plasma cells or large mononuclear leucocytes.

Figures A 1, 2, 3 and figure 6 represent cells from the muscle lesions in trichinosis (case XXXI), Figures B 1, 2, 3 and 4 as well as figures 5 and 7 are drawn from cells in an oedematous tubercular lymph gland (case XXVIII).

# EOSINOPHILIA IN PELVIC LESIONS AND IN THE VERMIFORM APPENDIX.

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IN the routine microscopic examination of all tissues removed at operations in the gynecological service of the Lakeside Hospital, cells with eosinophilic granulations have frequently been observed in the tissues, especially in inflammatory conditions. In this laboratory their occurrence was first noted in the gynecological department in 1898, and subsequently so many instances were observed in all the departments of the laboratory that Howard and Perkins[1] were able to report a large number of cases. The present article deals with the material of the gynecological department alone.

Howard and Perkins in material from 825 consecutive operations in the different services of the hospital found eosinophiles in the tissues of 108 cases, or 13 per cent. Of these 80, or 74 per cent., were inflammatory; 24 cases were acute and 56 were chronic; 9 were tuberculous and 9 were syphilitic. In 120 consecutive autopsies eosinophiles in larger or smaller numbers were found in organs showing pathological changes in 27 instances. They occurred in the spleen, liver, stomach, intestines, kidney, heart, lung, thymus, lymph glands, and skeletal muscles.

These findings appear to warrant the conclusion that eosinophiles take an active part in many inflammatory processes, more especially appendicitis, pyosalpinx, and ovarian abscess, as well as in many cases of carcinoma showing inflammation; that they are often associated with polymorphonuclear neutrophiles and almost invariably with plasma cells; that their development from plasma cells and mononuclear leucocytes could be traced in many instances. These writers are of the opinion that the eosinophiles found in the tissues have usually emigrated from the vessels, but that in a certain proportion of cases they are formed in the lesion by transition from plasma cells and mono-

[1] Johns Hopkins Hospital Reports, vol. x.

nuclear leucocytes. Their article contains a careful review of the literature, of which two references are here applicable.     .

Przerwoski[1] noted them in 4 cases of carcinoma of the portio vaginalis, occurring in the connective tissue, in the carcinoma cell nests, and in the bloodvessels. He counted as many as five, ten, or fifteen in a single D D Zeiss field.

Feldbausch[2] found eosinophiles in uterine carcinoma and mammary cancer with acute mastitis, in metastases in lymph glands secondary to epithelioma of the vulva, in epithelioma of the bladder and of the lip, and in some sarcomata and lymphosarcomata. He gives many references, and quotes similar cases noted by Rimbach and Neusser.

As regards the technique employed, the majority of the tissues were fixed and hardened in Orth's fluid (Müller's fluid, 9 parts; 40 per cent. formaldehyde solution, 1 part), the best results being obtained after hardening in this for a week; they were then embedded in celloidin and stained with hæmatoxylin and eosin. The eosinophiles are also readily demonstrated after hardening with mercuric bichloride, formalin, Zenker's or Müller's fluids, and staining with hæmatoxylin and eosin, or with eosin followed by polychrome methylene blue or carbolic toluidin blue, or with the Biondi-Heidenhain triple stain. Tissues hardened in alcohol fail to show the eosinophiles satisfactorily. In specimens hardened in Orth's fluid and stained with methylene blue alone the granulations of the eosinophiles, although unstained, are plainly visible with the higher powers, while in alcohol hardened preparations, even after staining with eosin, they cannot be seen. Fine scrapings of the appendix mucosa, which almost invariably shows eosinophiles, were dropped into warm absolute alcohol with no better result. Parallel pieces of the same appendix were hardened in the usual reagents and stained as uniformly as possible. The eosinophiles were well shown after employing Orth's fluid, formalin, Zenker's and Müller's fluids, and mercuric bichloride, but they could not be found after using alcohol. The same results were obtained in a number of cases of thickened pyosalpinx when adjacent pieces of each were hardened in the different fluids.

Very satisfactory results were obtained with suitable tissues hardened in Orth's fluid and stained with eosin, followed by Unna's polychrome methylene blue or carbolic toluidin blue. The bacteria and nuclei are stained blue; the eosinophiles are very prominent, and are readily distinguished from the polymorphonuclear neutrophiles, whose protoplasm takes a slight pinkish tinge, and from the mast cells, whose large granulations take the basic stain, being lilac-colored and darker than the bright-red eosinophilic granulations.

[1] Przerwoski. Centralbl. für Allgem. Patholog. und Path. Anatomie, 1896, vol. vii. s. 117.
[2] Feldbausch. Virchow's Archiv, 1900, clxi.

In inflammatory conditions the eosinophilic infiltration is usually most marked in suppurative cases or in the subacute stage. It occurs also in some recent acute and in chronic cases. These cells play a part in general cellular infiltrations in which polymorphonuclear neutrophiles, small round cells or lymphocytes, plasma cells, and mast cells also participate. The number of the eosinophiles varies within wide limits. Many of our cases showed them in the tissues, but in such small numbers that we have not included them in our list, while in others they were very numerous. Przerwoski[1] found as many as five, ten, or fifteen in a D D Zeiss field, but in several cases in selected areas we have counted as many as 250 in the smaller field of a 1/12 oil-immersion with an Oc. 4. They are usually polymorphonuclear, although mononuclear forms are also found. As a rule, they are spherical, but frequently are elongated and fusiform in shape, lying between the connective tissue or smooth muscle cells. Some of these fusiform cells may have but a few eosinophilic granulations and be mononuclear, the nucleus being vesicular and resembling those in the adjacent connective tissue cells. All intermediate forms between these and the polymorphonuclear spherical eosinophiles are seen, suggesting the possible formation of connective tissue cells from the eosinophiles, or *vice versa*. In such areas Howard and Perkins have traced the development of eosinophiles from smooth muscle fibres, and have shown that eosinophiles may be derived from plasma cells and large mononuclear leucocytes, and describe a progressive series of cells intermediate between these. We have observed these forms, but we have also frequently seen a similar series of cells intermediate in type between the plasma cell and the mast cell of the tissues, especially in the appendix mucosa, stained with Unna's polychrome methylene blue, carbolic toluidin blue, or either of these after eosin. The first stage is the formation of fine granulations in the plasma cell, which gradually become larger and stain more deeply until the typical mast cell of the type found in the tissues is reached. Whether or not this be an indication of the development of mast cells from plasma cells, or *vice versa*, the demonstration of an intermediate series of cells is at least of interest.

The pathological material upon which these observations are based was all obtained from the first 500 consecutive operative cases in which tissues were removed in the gynecological service of the Lakeside Hospital. In 145 of these cases infiltration with eosinophiles was found. The tissues from 261 of the 500 cases were hardened in alcohol, and therefore would not have shown eosinophiles even had they been present; 248 of these 261 cases supplied endometrium alone or with portions

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[1] Przerwoski. Loc. cit.

of the cervix. There are left, then, only 104 cases in which appropriate fixing agents were employed and in which eosinophiles were absent or found only in small numbers. The majority of these were chronic inflammatory cases.

The 145 cases with eosinophilic infiltration showed the following pathological conditions, which are arranged in the order of their frequency, the numbers indicating the number of cases in which each condition was found. The total would greatly exceed the number of cases, from the fact that several different pathological conditions showing eosinophilic infiltration often occurred in the same patient.

| | | | |
|---|---|---|---|
| Appendix, normal and diseased | . 56 | Omentitis . . . . . . . | . 4 |
| Pyosalpinx . . . . . | . 54 | Tubal pregnancy . . . . | . 8 |
| Salpingitis . . . . . | . 33 | Normal corpus luteum . . . | . 8 |
| Ovarian abscess . . . . | . 25 | Sarcoma uteri . . . . | . 8 |
| Perioöphoritis . . . . | . 17 | Interstitial cervicitis . . . | . 8 |
| Corpus luteum cyst . . . | . 12 | Fibro-adenoma of the breast . | . 2 |
| Congestion of the Fallopian tube | . 11 | Proctitis . . . . . . | . 2 |
| Endometritis interstitialis . . | . 10 | Malignant adenoma uteri . . | . 1 |
| Carcinoma of the cervix . . | . 11 | Suppurative metritis . . . | . 1 |
| Hydrosalpinx . . . . | . 6 | Fibromyoma uteri . . . . | . 1 |
| Oöphoritis . . . . . | . 4 | Syphilitic elephantiasis of the vulva | . 1 |

These conditions will now be considered more in detail.

*Pyosalpinx* was the most frequent inflammatory condition showing eosinophilic infiltration. In the 500 cases pyosalpinx was found 62 times, being usually bilateral; 54 of these cases showed eosinophiles in the tissues in large numbers; in 4 cases only a few of these cells were found, in 2 of which the tissues were imperfectly hardened, while a third showed marked eosinophilic infiltration in the other tissues removed; in 4 cases they were absent, the tissues in 3 of these having been hardened in alcohol.

The infectious agent in the majority of these cases, and in fact in most pelvic inflammatory conditions, was undoubtedly the gonococcus. In a number of instances typical gonococci were found on cover-slip examination of the pus and also in stained sections of the tissue; in many others, although the history was extremely suggestive, cover-slip examination and cultures of the pus proved negative, thus confirming the statement that in many cases the pus is either sterile or of slight virulence. Streptococcus pyogenes, bacillus mucosus capsulatus, staphylococcus pyogenes albus, and bacillus tuberculosus were the causal agents in some of the above cases.

In pyosalpinx the eosinophiles are most numerous in the muscularis, especially where this is considerably thickened. Here they are often seen assuming a spindle form and crowded into rows between the muscle and connective tissue cells. They are seen more sparsely in the stroma of the folds, in the purulent exudate, and in the vessels; they are never

so numerous in the folds as in the muscularis. In the vessels the leucocytes are often increased in number, but the percentage of eosinophiles is usually about normal, although on account of their more prominent appearance the proportion seems increased. Since the histological findings in most of these cases are very similar, a short description of one will suffice.

*Gynecological Pathological, No. 465.* Right perioöphoritis and pyosalpinx; left ovarian abscess and pyosalpinx. The left tube, 8 cm. in length, is much thickened, convoluted, and occluded. The lumen is distended with pus showing typical gonococci; the outer surface of the tube is covered with dense adhesions.

Microscopically the lumen contains a quantity of pus, gonococci being seen in some of the cells. The folds of the mucosa are numerous, showing a complex arrangement, but only a few adhesions. As a rule, they are greatly thickened and swollen, exhibiting dense cellular infiltration, with polymorphonuclear neutrophiles, lymphocytes, plasma cells, eosinophiles, and mast cells. The epithelium is almost everywhere intact, but is pale, swollen, and cuboidal, being scarcely distinguishable from the connective tissue cells of the folds. The cilia are usually missing, and numbers of leucocytes are found between the epithelial cells. On the more normal folds the epithelium is intact, almost normal, and shows cilia.

The muscularis is greatly thickened. The muscle cells are pale and swollen. There is a considerable increase of connective tissue and a diffuse cellular infiltration, especially with the eosinophiles, which frequently exceed 10 per cent. of all the cells in the field. Large numbers of polymorphonuclear neutrophiles, lymphocytes, and plasma cells, with fewer mast cells, are also found. The peritoneum is found beneath thick adhesions, where it forms atypical groups of pale, swollen cells.

*Salpingitis,* without pus formation, showed eosinophilic infiltration in 33 cases; 6 of these, although diagnosed as acute salpingitis, contained microscopically a small amount of purulent fluid in their lumina, and might come under the head of pyosalpinx; in all 6 the eosinophiles were found only in the mucosa and in small numbers, their favorite site, the muscularis, being almost normal in appearance. In salpingitis the eosinophiles are usually less numerous than in pyosalpinx, and occupy the wall of the tube in subacute cases. In many cases of chronic or "'healed" salpingitis all acute cellular infiltration had disappeared, and hence eosinophiles were absent. The following case is instructive:

*Gynecological Pathological, No. 305.* Supravaginal hystero-salpingo-oöphorectomy for multiple fibromyomata uteri. Both ovaries and tubes macroscopically normal. Microscopically, in the right tube the lumen is empty; the mucosa is normal except for slight eosinophilic infiltration in some of the folds, which are numerous and show a normal arrangement. The surface epithelium is intact, the cells being columnar and ciliated. The muscularis shows very marked cellular infiltration,

almost entirely with polymorphonuclear eosinophiles, which are usually
accumulated in masses in the connective tissue between the muscle
bundles. In some fields of a 1/12 oil-immersion lens with Oc. 4, over
90 per cent. of all the cells seen are eosinophiles, as many as 250 being
counted in one such field without change of focus, although an adjoining
field often shows a total absence of them. This infiltration is entirely
missing in about one-third of the muscularis encircling the mucosa, and
in the other two-thirds no other pathological change is found. If it
were not for the actual presence in the tissues of the leucocytes a diag-
nosis of congestion would have been made instead of acute salpingitis.

*Congestion* due to traumatism at operation was found in tubes present-
ing a normal appearance, but which were removed with uterine fibro-
myomata, ovarian cysts, or some condition not involving the tube itself.
Microscopically the only change found in these cases is a congestion of
the vessels, with an increased number of leucocytes within their lumina.
The eosinophiles, while actually more numerous than normal, preserve
the usual ratio to the other leucocytes, although, owing to their more
prominent staining, the former appear increased. In all cases showing
such congestion the eosinophiles were sufficiently increased to attract
attention.

*Hydrosalpinx* was present in 23 of the 500 cases. In the majority of
these the changes were slight in degree and chronic, all acute cellular
infiltration having disappeared. This would readily account for the
fact that in only 6 cases were eosinophiles demonstrated.

*Tubal pregnancy* was found 5 times. In 3 there was moderate
eosinophilic infiltration; in another but few were found, the condition
being very chronic; a pyosalpinx, however, upon the other side showed
abundant eosinophilic infiltration. The tissues from the fifth case were
hardened in alcohol, and showed no eosinophiles.

*Ovarian abscess* was present in 27 cases, in some of which the condi-
tion was bilateral. Eosinophiles were seen in large numbers in the
abscess wall in all but 2 cases; in these the tissues had been hardened
in alcohol. Although in many of these cases there was a definite gonor-
rhœal history, the specific organisms could rarely be demonstrated. The
streptococcus pyogenes was found in 2 cases. One case only will be
quoted, the others presenting very similar findings.

*Gynecological Pathological, No. 394.* Left perioöphoritis and salpin-
gitis; right ovarian abscess and pyosalpinx. The right ovary—5 x 3.5
x 2 cm. — is of soft consistence, and shows a number of surface
adhesions. On section, an abscess sac is found in its interior. The
right tube is occluded, filled with pus, and densely adherent to the
ovary; together they weigh 31 grammes. Microscopically, the medulla
of the ovary is for the most part replaced by an abscess which appears
to have formed in a corpus luteum. The abscess wall is abundantly
supplied with small vessels, and shows dense cellular infiltration,
especially with eosinophiles, but also with polymorphonuclear neutro-

philes, lymphocytes, plasma cells, and fewer mast cells. The eosino-
philes are most numerous in the abscess wall about midway between the
inner necrotic border and the sound tissue outside. They give a red-
dish tinge to the tissue when seen with the lower powers, and in selected
areas with a 1/12 oil-immersion lens and a No. 4 ocular they sometimes
represent 60 to 75 per cent. of all the cells, as many as 150 having been
counted in one such field. These cells are also found in less numbers
in the pus within the abscess cavity, in the cortex and tunica albuginea,
and within the vessels.

*Perioöphoritis* representing either an acute exudation or chronic ad-
hesions was found in 121 cases. The majority of these were chronic,
and showed no acute cellular infiltration. Eosinophiles were found in
only 17 of the acute or subacute cases, often associated with pyosalpinx.

*Oöphoritis* showing eosinophilic infiltration was found in only 4 cases.

Excluding ovarian abscess and perioöphoritis, cellular infiltration of
the ovary itself is uncommon, the inflammatory process being held in
check apparently by the dense tunica albuginea, as is shown in many
cases of acute perioöphoritis, where the cellular infiltration is found only
in the exudate upon the surface.

*Corpora lutea* of normal appearance in three cases showed a number
of eosinophiles associated with the usual increase of the connective-
tissue elements in the later stages of the corpus luteum.

*Corpus luteum cysts* frequently show a slight cellular infiltration in
their walls which can scarcely be termed an oöphoritis. In 12 such
cases eosinophiles formed a considerable proportion of the infiltrating
cells. · Some of these cases probably represented enlargements of the
Graafian follicles, with loss of the membrana granulosa, as it is fre-
quently impossible to differentiate the two conditions.

*The endometrium* showed eosinophiles in small numbers in 10 cases
of interstitial endometritis; in interstitial inflammation of the cervix
they were found 3 times. These numbers seem small, but the majority of
these tissues was hardened in alcohol, since it is difficult to separate
the clot from the tissue if Orth's fluid be used. At present, however,
we employ formalin. Of the 500 cases, in 248 the tissues represented
endometrium alone or with portions of the cervix hardened in alcohol.

*Metritis.* Six cases of very slight metritis did not show eosinophiles,
but in 1 of suppurative metritis they were numerous. The following
is an illustrative case:

*Gynecological Pathological, No. 295.* Uterus septus partialis; acute
interstitial endometritis; suppurative metritis; left tubo-ovarian ab-
scess; right salpingitis and oöphoritis; adherent appendix. The uterine
wall upon the left side was riddled with small abscesses, the pus from
which showed streptococci on cover-slips and cultures. Eosinophiles
were very numerous in the abscess wall.

*Carcinoma* of the cervix occurred in 16 of the 500 cases. In only 1 of these was a hysterectomy performed, the remaining cases being so far advanced as to warrant merely a palliative curetting, which in some cases was repeated at a subsequent date. Eosinophiles were found in large numbers in 11 of the 16 cases; they were absent in 5, in 2 of which the tissues were hardened in alcohol. The favorite seat of the eosinophiles is along the advancing margin of the growth. One instance will be cited.

*Gynecological Pathological, No. 319.* Vaginal hysterectomy for carcinoma of the cervix occurring in a nullipara. Microscopically in this specimen the cell nests as well as the interstitial connective tissue show dense eosinophilic infiltration, most intense along the advancing margin, where they give the tissue a reddish color when seen with the lower powers. In some fields of a 1/12 oil-immersion lens more than 90 per cent. of the cells seen are eosinophiles.

*Malignant adenoma* of the body of the uterus was found in the material from two operations upon the same patient. Curetting was first done for diagnosis, and subsequently hysterectomy was performed. The disease was in a very early stage, and did not involve the muscularis; the eosinophilic infiltration was slight. The condition corresponded with the malignant adenoma described by Gebhard[1] as distinguished from adenocarcinoma.

*Sarcoma Uteri.* Three cases occurred, and have been reported in a recent article.[2] In all, eosinophiles were found among the sarcoma cells and in the muscularis of the uterine wall near the advancing neoplasm. They were not so numerous as in carcinoma of the cervix.

*Fibromyomata uteri* were represented in 25 of the 500 cases; in 1 eosinophiles were found associated with areas of hyaline degeneration of the tumor.

*Chronic syphilitic inflammation of the labium minus*—the so-called elephantiasis syphilitica—occurred once in our series. There was a great increase of fibrous connective tissue, marked endarteritis, and considerable cellular infiltration, in which eosinophiles occurred in moderate numbers.

*Fibro-adenomata of the breast* were removed in 2 cases as supplementary procedures to other operations. They were both small, and showed areas of myxomatous degeneration. No inflammatory process was found microscopically, but in Gynecological Pathological, No. 475, a typical intracanalicular fibro-adenoma; these cells were fairly numerous, usually mononuclear, and scattered throughout the stroma. The other case showed but few.

*Vermiform Appendix.* This was removed frequently as a secondary procedure to some other abdominal operation. In many of these cases

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[1] Gebhard. Patholog. Anat. der Weibliche Sexualorgane, 1898.
[2] Weir. American Journal of Obstetrics and Diseases of Women and Children, 1901.

it showed but slight pathological change, such as light surface adhesions, concretions in the lumen, or sharp twists from shortening of the mesoappendix. Upon microscopic examination the greater number of these appeared perfectly normal. The occurrence of eosinophiles in the mucosa of the normal or diseased appendix is almost invariable, and as a number were examined the findings are included in this paper.

In the 500 cases the appendix was removed 69 times, and eosinophiles were found in considerable numbers in 56. Their absence in the remaining 13 is explained by the fact that in 11 the lumina were occluded, and the mucosa, in which the eosinophiles are found, was entirely replaced by connective tissue; the remaining 2 specimens were hardened in alcohol. Of the 56 showing eosinophiles 47 were microscopically normal, although 4 of these contained firm concretions in the lumen and another contained two grape-seeds; 5 showed inflammation in varying degree, 1 contained pus, the remainder showing periappendicitis. In 2 myxomatous degeneration of the mucosa was found, 1 of these being quite cystic. Another case showed cystic dilatation above a narrow constriction, and in the remaining case the appendix was occluded, the epithelial elements were entirely lacking, but some of the lymphoid tissue still remained and showed eosinophiles. One case will be mentioned.

*Gynecological Pathological, No. 393.* Left salpingo-oöphorectomy and appendectomy. The appendix, 8 cm. in length, was perfectly normal except for a sharp flexure due to a shortening of the meso-appendix. Microscopically a considerable proportion of the cells composing the stroma of the mucosa are polymorphonuclear eosinophiles. They represent fully 10 per cent. of all the cells, and in some fields with a 1/12 oil-immersion lens they reach 30 to 50 per cent. They are most numerous in the deeper layers around the bases of the tubular glands, but are absent in the lymphoid nodules. They are usually polymorphonuclear, but a few are mononuclear. They are, as a rule, spherical or oval in shape, but also flattened or irregular in outline. Owing to the whole cell being stained, their number seems even larger than it really is. Polymorphonuclear neutrophiles are very scanty in the mucosa, but many plasma cells and some mast cells are found.

*Rectum.* In 2 cases with dense adhesions portions of the rectal wall were torn away at operation. Microscopically these showed large numbers of eosinophiles in the mucosa, and also forming part of a diffuse cellular infiltration throughout the whole bowel wall. Mast cells are found in much smaller numbers.

*Omentum.* Frequently at operation small portions of the torn or adherent omentum required resection. In 7 cases it showed an inflammatory condition. Eosinophiles were found in considerable numbers in 4, in small numbers in 1. In the remaining 2, where the inflammatory condition was very slight, they were missing.

*Circulatory Eosinophilia.* An increased number of eosinophiles in the circulating blood is said to occur in certain pelvic lesions, 4 per cent. of all the leucocytes being considered the maximum normal number of the eosinophiles.

Cabot[1] says that in carcinoma of the uterus with a leucocytosis the eosinophiles in the blood are not always decreased (as they are in many other leucocytoses), nor are they increased except when bone metastases occur. He also states that in gonorrhœal infection and in many ovarian tumors there is frequently an eosinophilia, while in most leucocytoses there is a decrease of eosinophiles.

Ewing[2] also states that there may be an eosinophilia in gonorrhœal infection.

Ehrlich and Lazarus[3] admit a moderate eosinophilia in some malignant tumors.

Vosswinckel,[4] who made differential counts in a large number of cases of disease of the female genitalia, concluded that:

1. A circulatory eosinophilia is absent in diseases of the tube alone. In pus cases there may be an increase in the polymorphonuclear neutrophiles, but no myelocytes are found. In 30 cases of fibromyomata a circulatory eosinophilia did not occur, nor was it noted in 23 cases of endometritis. In both of these latter conditions, however, a leucocytosis may occur.

2. In all severe diseases of the ovary, with fever, except carcinoma of the ovary, there is a circulatory eosinophilia.

3. In the majority (10 out of 18) of cases of large ovarian cysts and suppuration of the ovary causing extensive degeneration there is a circulatory eosinophilia, and myelocytes are also found.

4. In carcinoma of the uterus the eosinophiles in the blood may be increased, normal, or decreased, there being no difference between mild and severe cases.

Vosswinckel also quotes the following:

Neusser found in ovarian disease that the eosinophiles were increased, and that the myelocytes, which are not found in normal blood, are also found.

Kopp in 5 out of 16 cases of pelvic disease found an undoubted circulatory eosinophilia.

Zappert found the eosinophiles in the blood increased in 2 cases of carcinoma of the uterus and in 1 case of sarcoma of the ovary; decreased in 1 carcinoma of the ovary.

[1] Cabot. Clinical Examination of the Blood.
[2] Ewing. Clinical Pathology of the Blood, 1901.
[3] Ehrlich and Lazarus' Die Anämie. Nothnagel's specielle Path. und Therapie, 1901.
[4] Ueber das Vorkommen von eosinophilian Zellen und Myelocyten in menschlichen Blute, Monats. für Geburtshülfe und Gyn., 1899.

Reinbach in 40 cases of malignant tumors found the eosinophiles in the blood lessened in only 1 case of carcinoma of the ovary and stomach.

Our own observations on this point are limited, but as far as they go we have found that more than 4 per cent. of eosinophiles in the blood in pelvic diseases is quite uncommon. In most instances the counts were made in the inflammatory conditions associated with leucocytosis, and in most of them the eosinophiles were decreased in number, confirming Cabot's statement. In 29 of the cases showing eosinophilic infiltration of the tissues 48 differential counts were made, and in only 3 cases was a circulatory eosinophilia found.

*Gynecological Pathological, No. 349.* Bilateral chronic hydrosalpinx and perioöphoritis. Leucocytes, 4800; eosinophiles, 5.12 per cent.

*Gynecological Pathological, No. 124.* Right perioöphoritis and hydrosalpinx; left perioöphoritis and pyosalpinx. The day before the operation the leucocytes were 20,000, with 4 per cent. of eosinophiles. Two days after operation the leucocytes had fallen to 12,000, with 5 per cent. of eosinophiles.

*Gynecological Pathological, No. 63.* Left ovarian abscess and pyosalpinx (streptococcus); right perioöphoritis and salpingitis. Leucocytes, 8666; eosinophiles, 5 per cent.

Four per cent. of eosinophiles occurred but once, in a case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 16,900; 3 per cent. of eosinophiles was found twice, in one case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 9740, and in a case of bilateral gonorrhœal pyosalpinx, with a leucocytosis of 9260.

In the remaining 23 cases 41 counts were made. In 20 counts made in 12 cases the eosinophiles were 2 per cent. or a fraction over; in 11 counts made in 11 cases the eosinophiles were 1 per cent. or a little over; in 10 counts made in 10 cases the eosinophiles were below 1 per cent. In all examinations at least 400 leucocytes were counted, and in none were myelocytes found. These counts were nearly all made immediately before operation. In some cases subsequent examinations were made on the first and second days after operation. A considerable number of differential counts were made in cases in which no eosinophilic infiltration of the tissues was found or in which operation was refused. The only one of these showing an increase of eosinophiles in the blood was an advanced carcinoma of the cervix. In this case 7.5 per cent. of eosinophiles were found.

CONCLUSIONS. 1. Eosinophiles take a prominent part in the cellular infiltration associated with inflammatory and suppurative processes of the pelvic organs.

2. In such conditions they usually occur in the largest numbers in the subacute stage and associated with connective tissue hyperplasia.

3. Eosinophilic infiltration is found in most cases of carcinoma of the cervix and in almost all cases of pyosalpinx and ovarian abscess.

4. In inflammatory conditions of the endometrium eosinophiles occur in small numbers and in but few cases.

5. Eosinophiles represent a large proportion of the cells forming the stroma of the mucosa in the normal and the diseased appendix.

6. In inflammatory conditions of the pelvic organs associated with an eosinophilic infiltration of the tissues the percentage of eosinophiles in the circulating blood is rarely increased, and usually decreased.

I am much indebted to Dr. William T. Howard, Jr., Professor of Pathology, and Dr. Hunter Robb, Professor of Gynecology, for kindly advice and permission to make use of the pathological material.

# PRIMARY SARCOMA OF THE ESOPHAGUS AND STOMACH.*

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## PRIMARY SARCOMA OF THE ESOPHAGUS.

The fact that there are only eleven cases recorded in the literature shows that this affection is rare. Most of the cases have been regarded as pathological curiosities and were reported by the following authors: Chapman, 1877; Targett, 1889; Stephan, 1890; Shaw, 1891; Rolleston, 1893; Albrecht, 1895; Ogle, 1896; Livingood, 1898; Gastpar, 1900, and Stark, 2 cases, 1900. Besides these, Perry and Shaw, in an article on malignant tumors of the stomach, allude to two cases of sarcoma of the esophagus without, however, giving either clinical or pathologic data.

To the previously reported cases I am able to add another, that of a smooth muscle cell sarcoma of the lower end of the esophagus. The history is as follows: S. B., aged 51, was admitted to the Cleveland City Hospital service of Dr. Hoover, August, 1900, complaining of vomiting and difficulty in swallowing. He died a few weeks later of exhaustion.

*Clinical Diagnosis:* Carcinoma of the esophagus. Autopsy by Dr. Moore, resident pathologist.

*Anatomic Diagnosis:* Carcinoma of the lower end of the esophagus, with metastasis in the cardiac end of the stomach, slight chronic interstitial nephritis, brown atrophy of the

heart, emphysema and pigmentation of the lungs with bron-
cho-pneumonia.

The body was 157 cm. long and markedly emaciated. The
surface of the body was free from scars, abrasions and new
growths. The superficial lymph glands were not enlarged.
As the esophagus and stomach are the only organs showing
lesions of present interest, the description of the other organs
is omitted.

*Esophagus:* The organ is of normal size and appearance
from its beginning to within 12 cm. of its cardiac end. At
this point its wall is much thickened, and its mucous surface
is the seat of irregular ulcers, covered with grayish necrotic
material. The surface is irregular, but there are no polypoid
masses projecting into the lumen. On section the wall is
rather thicker than usual, firm and dense in consistency,
and pale in color. The cardiac orifice of the stomach is nar-
rowed, but admits the little finger with ease.

*Stomach:* The stomach is of ordinary size and appears
normal throughout, except for the thickening of the cardiac
orifice above described and for the presence near the latter
of a nodular tumor, 7 cm. in its greatest diameter. On sec-
tion this mass is seen to be beneath the mucosa. It is dense
and firm and on section is glistening in appearance. Some
of the lymph glands near the stomach are enlarged. There
are no other metastases.

*Microscopic Examination of Esophagus and Stomach:* Sec-
tions made at various points through the wall of the esophagus,
including the tumor, show in general the same appearances.
The mucosa is fairly well preserved between the points of
ulceration. In some places it is necrotic and contains num-
bers of bacilli, some of which are large and stout. In other
places the mucosa is entirely replaced by a mass of fungoid
tissue. It is composed of a fairly vascular fibrous tissue con-
taining a number of larger and smaller areas of large spindle-
shaped, large and small round, and many giant cells, which are
supported by a variable amount of intercellular substance.
There is no distinct alveolar structure, but a semblance of this
occurs when masses of these cells occupy dilated vessels. The
cells are often seen infiltrating the denser fibrous tissue.
The nuclei of the tumor cells are large and vary much in
shape, but are usually oval; they are often elongated, and
even fusiform. They are usually vesicular and many of them
contain fine chromatin granules. Some nuclei are dense and
stain diffusely and deeply with hemotoxylin and methylene
blue. Some swollen nuclei contain small nucleoli. Nuclear
figures are very numerous. The sarcomatous tissue is not
diffuse, but, especially at the borders of the growth, occurs in
patches. When, as is often the case, they occupy dilated lymph

or blood vessels, the cells are usually large and often round, but even here long fusiform cells with long swollen vesicular nuclei are seen. In a few places the cells are arranged in concentric layers, and the cells of the inner layers are flattened and often show hyaline degeneration. The growth is best marked in the muscularis, all the coats of which are involved. (At the seat of the tumor only smooth muscle tissue is to be found.) In this tissue the most characteristic appearances of the growth are found. It consists of larger and smaller areas composed largely of long spindle-shaped cells with long swollen oval or fusiform nuclei. The cells and nuclei are often very large. The cells lie in parallel rows, usually separated by a small amount of intercellular tissue, which is, however, often absent or invisible. There is a striking resemblance between these cells and their nuclei and the muscle cells and nuclei of the neighboring tissue. The tumor cells nearest the muscle tissue very closely resemble those of the latter. They are narrower and have long oval or fusiform rather deeply staining nuclei. In most places it is easy to trace all gradations between the large tumor cells and the narrow muscle cells with thin deeply staining nuclei. The stages in the development of the muscle cells into tumor cells is as follows: Along the advancing border of the growth the nuclei of some of the muscle cells swell and become more vesicular; later the nuclei become more swollen and develop fine chromatin granules. At the same time the cell body becomes thicker and its ends become somewhat rounded, and finally develops into a modified fusiform or even oval shape. Such cells can be found among unchanged muscle cells at quite a distance from the new growth. They are not infrequently found in isolated groups. In the sarcomatous tissue there are a number of large round cells with oval or round vesicular nuclei containing fine chromatin granules. Sections stained with Weigert's elastic tissue stain show little if any newly formed elastic tissue. As far as can be seen the fibrous tissue of the submucosa and of the muscularis plays no part in the tumor formation. Many of the larger sarcomatous areas show marked necrosis, with nuclear fragmentation. In the tumor tissue and at its border there are numerous polymorphonuclear eosinophiles. This tumor, then, is a mixed cell sarcoma apparently divided solely from the smooth muscle tissue of the esophagus.

Sections of the wall of the stomach made through the nodule show atrophy and superficial necrosis of the mucosa, which is entirely lost in places. In other places it is infiltrated with small round cells. The submucosa is in general free, but here and there shows the same round cell infiltration. The muscularis is the seat of an extensive invasion of a

new growth in every way similar to that described in the esophagus. In most places the tumor cells are situated in dilated vessels. In some places the tumor tissue infiltrates the muscularis and a number of areas are to be seen in which the muscle cells take part in the tumor growth and· show the same changes noted in the esophagus. In many of the muscle cells near the new growth there are large vacuoles.

Sections of the enlarged lymph glands show a new growth similar to that of the esophagus and stomach. There is, however, marked necrosis.

*Revised Diagnosis:* Primary myosarcoma of the esophagus, with metastases in the stomach and neighboring lymphatic glands.

Until Livingood's paper, in 1898, sarcoma of the esophagus was regarded as a pathologic curiosity and, on account of its rarity, of no special clinical importance. Livingood analyzed the cases reported to the date of his article and added a well-studied case with a full clinical history. He concludes that there is clinically no essential difference between sarcoma and carcinoma of the esophagus. He further notes that the advance of sarcomatous tumors of the esophagus is more rapid than carcinoma, being fatal within nine months from the first symptoms; that widespread metastases and the location of metastases are as uncommon and indefinite as in carcinoma, and finally, that the mode of termination is the same in both. Livingood found eleven cases of carcinoma and one case of sarcoma of the esophagus in one thousand consecutive autopsies. He suggests that the apparent rarity of sarcoma is due to a lack of careful histological study of esophageal tumors.

Stark, in the most recent and complete article on esophageal sarcoma, reports two cases and analyzes the clinical symptoms of the affection. In regard to the differential diagnosis between sarcoma and carcinoma of the esophagus, he states that age has little influence if the case of Stephan (a 4-year-old child) is excepted, but that in an individual under 25 years of age sarcoma is much more probable than carcinoma. He thinks that the most important symptom is pain, which in carcinoma may be lacking for months, and when it does occur is rarely of the intense stabbing character observed in sarcoma; the pain in carcinoma is usually most marked after eating, and in sarcoma while fasting, especially at night. He further states that the pain in sarcoma is

back between the shoulder blades, which is uncommon
in carcinoma. He also points out that the duration of
the disease is shorter in sarcoma; in one of his cases
death occurred in ten weeks after the first symptoms of
dyspepsia.

A critical study of the twelve recorded cases (includ-
ing my case) of sarcoma of the esophagus brings out the
following information:

*Age.*—Youngest, 4 years (lympho-sarcoma, Stephan); 25
years, one case; 38 years, one case; 41 years, one case, 45 years,
one case; 50 to 55 years, five cases, and 60 to 70 years, two
cases. (The cases of Perry and Shaw are mentioned without
clinical or pathological data and are, therefore, useless for
generalization.)

*Situation of the Tumor.*—Lower part of the esophagus, 9
cases; upper part, 2 cases; not mentioned in 1 case.

*Morphology of the Tumors.*—Pedunculated or polypoid in 3
cases (Ogle, Albrecht and Stephan); diffuse tumor formation
with polypoid or nodular excrescences in 2 cases (Livingood
and Gastpar); tumor mass completely surrounding the lumen
in 5 cases (Rolleston, Gastpar, Stark—2 cases—and Howard);
not mentioned in 3 cases. More or less obstruction occurred
in nearly all cases; in some stenosis was complete. Ulceration
of the mucosa and of the growths occurred in 7 cases. Perfora-
tion of the esophagus occurred in 4 cases; into the trachea
twice (Shaw and Livingood); and with pleurisy and lung
inflammation twice (Rolleston and Stark).

*Histologic Characters of the Tumors.*—Lympho-sarcoma, 1
case (Stephan); round cell sarcoma, 4 cases (Shaw, Stark,
Stark, Rolleston); pure spindle cell, 2 cases (Ogle and Livin-
good); oval and spindle cell, 2 cases (Chapman and Targett);
alveolar, 1 case (Albrecht). Large mixed cell, 1 case (Gast-
par); muscle cell, 1 case (Howard).

*Metastases* were noted in 5 cases; in the neighboring
lymph glands, stomach, intestines, kidneys, adrenals, lungs,
liver, brain, etc., in 1 case (Stark); in the peripancreatic
lymph glands, the iliac bone and neighboring muscles, the
temporal bone and muscle, 1 case (Rolleston); in the neigh-
boring lymph glands and kidneys, 1 case (Shaw); in the
stomach and gastro-hepatic lymph glands, 1 case (Howard);
and in the liver, 1 case (Stark).

In one of Stark's cases the stomach contents were acid in
reaction, without, however, the presence of free HCl.

In 4 cases, no clinical diagnosis was made; in 3 cases it was
carcinoma, in 3 esophageal tumor; in one case periostitis of the
spinal vertebræ with extension to the esophagus, with peri-

gastritis; in 1 case there were no clinical symptoms referable to the esophagus. In this case—Albrecht's—the patient died of croupous pneumonia and at autopsy a pedunculated alveolar sarcoma was found in the esophagus.

*Conclusions.*—Analysis of the twelve recorded cases of sarcoma of the esophagus shows the following: 1. The disease is more common in males than in females, and at the period of life during which carcinoma most frequently occurs. It may, however, unlike carcinoma, occur in early life—between 4 and 25 years. 2. Nine of the twelve cases involved the lower half of the organ. 3. While the tumors usually nearly surround the lumen; in three cases they formed pedunculated or polypoid masses projecting into the lumen. 4. Symptoms of esophageal obstruction occurred in eleven of twelve cases. 5. There was perforation with involvement of the respiratory organs in four cases. 6. All the varieties of sarcoma except angio-sarcoma have been found. the round cell variety standing first in frequency—one-fourth of the cases. 7. Metastases occur rather frequently (five out of twelve cases), and in two cases were widespread. 8. The clinical diagnosis of esophageal sarcoma has not been made and there are no certain and constant diagnostic points between sarcoma and carcinoma of this organ, the clinical symptoms being necessarily very much the same and dependent upon the same conditions—obstruction and cachexia—in the two diseases. 9. As pointed out by both Livingood and Stark. sarcoma runs a more rapid course, and a fatal issue is to be looked for earlier than in carcinoma. The greater size of the sarcomatous growths is probably responsible for this. 10. The differences in the character, distribution, and period, of the pain in the two affections described by Stark, are not mentioned by other observers. It would prove a matter of considerable importance if his experience is confirmed.

### PRIMARY SARCOMA OF THE STOMACH.

A case of sarcoma of the stomach was recognized and reported as early as 1847 by Bruch, and Virchow described three cases in 1865. Although a considerable number of cases were reported, chiefly as pathologic curiosities, it was not until the classical article of Schlesinger, in 1897, that the subject assumed clinical import-

.ance. This author reported three personally observed
cases and collected 33 others from the literature. In
1898 Brooks reported a case and analyzed 15 others
which he collected from the literature. In the past six
years several cases have been reported by surgeons—
Hartley. Baldy, Capello, Cantwell and others—who have
removed gastric sarcomata at operation. The best of
the recent articles on gastric sarcoma is that of Dock, in
1900, who reported a carefully studied case, and col-
lected 13 additional cases from the literature, which.
added to the cases collected by Schlesinger, brought the
total number of known cases up to 50.

In a careful search of the literature I have been able
to add 7 cases to these, which, together with the 4
cases reported in this article, increase the total number
of cases to 61. I have taken considerable pains to criti-
cise the accuracy of the diagnosis in the cases collected
from the literature and have excluded all those in which
there was any apparent doubt in regard to the correct-
ness of the diagnosis of sarcoma. As several of the re-
ported cases have been found by accident in articles
under other titles, I am led to believe that this list does
not include all the recorded cases. All who write on the
subject must acknowledge a debt to Krüger, Schlesinger
and Dock. The disease is ignored in most of the text-
books on diagnosis, diseases of the stomach and path-
ology.

CASE 1.—Diffuse round cell sarcoma with atrophy and con-
striction of the stomach.

Female, aged 65 years, a patient of Dr. J. H. Lowman, to
whom I am indebted for the clinical history, complained of
nausea and vomiting for over a year before her death, which
occurred Jan. 12, 1896. She was weak and emaciated, but was
able to walk about the room three days before her death. No
mass could be palpated in the abdomen.

Clinical Diagnosis: Carcinoma of the stomach.

Autopsy: The body was that of a woman of ordinary size,
and was poorly nourished. The abdomen was distended. The
skin showed no scars, abrasions or new growths. The peri-
cardium, heart, aorta and large vessels showed no abnormali-
ties. The esophagus was normal.

Stomach: The stomach occupied its usual position. It was
very small, being about one-fourth its ordinary size. On
external examination it was everywhere hard, firm and in-
elastic. Midway between the cardia and pylorus the organ was

markedly constricted, roughly resembling an hour-glass in shape. On section its wall was everywhere greatly thickened, being from 1 to 3 or 4 cm. in thickness. At the point of constriction the lumen was 3 cm. in diameter. The mucosa, which was of a brownish-red color, was unbroken. The thickening of the stomach wall was due to the presence of a dense and firm grayish-white tissue, which had a rather homogeneous appearance. This tissue apparently did not encroach upon the mucosa, but involved the submucosa and muscularis, both of which coats were extensively infiltrated. The gastro-hepatic, mesenteric and retro-peritoneal lymph glands were enlarged and had the same appearance as the growth in the wall of the stomach.

The other organs showed nothing of present interest.

Sections of the stomach made of various portions showed in some places disintegration of the mucosa. In some places it had entirely disappeared. In all the sections examined, the submucosa was transformed into a fibro-cellular tissue composed of newly-formed fibrous tissue containing variable numbers of small round and oval cells. The cells showed no special arrangement, but often occurred in groups and masses and were always supported by fibrous tissue or by a fibrillar intercellular substance. The individual cells varied from 8 to 15 mikrons in diameter. They had a single round or oval nucleus which usually stained deeply and uniformly with hematoxylin. Some cells had paler nuclei. The cell bodies were usually round or slightly oval. A few spindle-shaped cells were seen. In all sections the muscularis was markedly invaded, in many places diffusely. All grades of invasion of this coat occurred from small islands of tumor cells to complete transformation into tumor tissue. The muscle tissue was pushed aside and infiltrated by the new growth. There was no evidence of proliferation of the muscle cells, which, so far as could be determined, played no part in the tumor formation. The origin of the tumor from the fibrous tissue of the submucosa was clear. A few blood vessels were found in the new growth. In no places was invasion of blood vessels made out. The amount of fibrous tissue present in some parts of the tumor warrants the term fibro-sarcoma. Sections of the lymph glands showed a growth in all respects similar to that of the stomach.

*Anatomic Diagnosis:* Small round and oval cell sarcoma of the stomach, primary in the submucosa, and infiltrating the muscularis. Constriction producing hour-glass shape of the stomach. Secondary sarcomatosis of the gastro-hepatic mesenteric and retro-peritoneal lymph glands. Anemia.

CASE 2.—Mixed cell sarcoma of the stomach with abscess formation in the tumor, with metastases in the neighboring lymph glands.

R. F., female, aged 46 years, was admitted to the Lakeside Hospital, Sept. 7, 1898, service of Dr. Dudley P. Allen (Dr. Nevison acting), complaining of anorexia, headache, pain, and swelling in the region of the spleen. There was no vomiting and no pain in the epigastric region. A large mass could be felt in the region of the spleen. Examination was otherwise negative. The urine contained a trace of albumin but no casts. The red blood cells were normal in number and appearance. A considerable leucocytosis was noted.

*Clinical Diagnosis:* Tumor of the spleen. The patient died 12 days after admission. Autopsy a few hours after death.

*Anatomic Diagnosis:* Primary mixed cell sarcoma of the stomach with abscess formation and peritonitis. No metastases. Edema and congestion of the lungs. Adenoma of the duodenum. Streptococcus pyogenes and Staphylococcus pyogenes aureus, and a short liquefying bacillus in the peritoneal exudate and abscess of the tumor of the stomach.

The body was 172 cm. long. The general nutrition was good. There were no scars, wounds or growths upon the surface of the body. There was bilateral enlargement of the thyroid. The chest was well shaped, the pleuræ negative; the lungs showed congestion, edema and emphysema, but were free from tumors. The pericardium, heart and aorta are without present interest. The abdomen was distended and very tympanitic. The abdominal wall contained a thick layer of fat; the muscles were pale. The parietal peritoneum was covered with a thin fibrino-purulent exudation. The coils of the intestine were bound together by recent fibrous adhesions, containing larger and smaller collections of creamy pus. The liver projected 4 cm. below the costal border in the mammary line. The under surface was adherent to the stomach, and the colon. The stomach was intimately bound to the surrounding structures, and was displaced downwards towards the left, so that its posterior surface lay over the left kidney. Its anterior wall was of ordinary size and appearance. The posterior wall was thickened. On the right side there was a ragged opening, 8x4 cm., between the peritoneal cavity and with a large cystic area in the posterior wall of the stomach.

*Stomach:* On removal and section the stomach contained foul-smelling yellowish material. The cubic capacity of the organ was reduced, while its bulk was markedly increased. The anterior wall was normal in appearance. Near the lesser curvature, and affecting nearly the whole of the posterior wall, there was a tumor mass 20x16 cm. which varied from 0.5 to 8 cm. in thickness. Near the lesser curvature there was a fungus-like mass, 6x8 cm. in breadth and length, which protruded into

the lumen of the stomach. This protuberance was irregular
in outline and ulcerated, and covered with a foul-smelling yel-
lowish pus. The tumor did not extend to or involve the pylorus,
which was quite soft. The tumor lay beneath the mucosa
everywhere except at the ulcerated area. At the cardiac end
of the tumor there was a cyst 7x4 cm., and at the pyloric end
a similar cyst 6x5 cm.; between these there was a larger cyst,
communicating with the other two. These cysts contained
fluid and necrotic material. The larger cyst communicated
with the peritoneal cavity. The tumor varied very much in
thickness, the cyst walls being from 1 to 3 cm. thick. The
tumor involved the submucosa and invaded the muscularis and
mucosa irregularly. On section it varied much in consistency,
in some places it was soft, while in others it was dense and
firm. On the right side of the stomach near the tail of the
pancreas, there was a nodular mass, apparently an enlarged
lymph gland, measuring 8x4 cm., which on section had the
same appearance as the growth in the stomach, and contained
a cyst 3x2 cm. in size. The neighboring lymph glands were
swollen. The posterior wall of the stomach was bound to the
pancreas, which was not, however, invaded by the tumor. The
duodenum was markedly congested; 8 cm. below the pylorus
there was a small nodule, 1.5 cm. in diameter, situated in the
submucosa. The rest of the intestines showed nothing abnor-
mal., The other organs showed nothing of present interest.

Sections of the stomach made at a distance from the tumor
showed nothing abnormal. Sections from various portions of the
tumor all showed much the same structure, the tissue being com-
posed of rather large round, oval and spindle-shaped cells of the
connective-tissue type, and with relatively large nuclei. The
cells were not arranged in alveoli, but a supporting connective-
tissue could be made out. In some places, especially at the
borders, the tumor was fibro-cellular, while in others it was
markedly cellular in structure. Larger and smaller areas of
necrosis were found. Sections taken from the margins of the
cysts showed marked necrosis, with nuclear fragmentation. In
this material there were large and small clumps of large bacilli.
In a few places there was an intimate relation between the
tumor cells and the adventitia of arteries and veins, suggestive
of the vascular origin of the former. These areas were always
isolated. In other places, at a considerable distance from the
main tumor, there were small irregular islands of typical
sarcoma tissue and apparently springing from the connective
tissue of the submucosa. The tumor was situated in the sub-
mucosa and invaded the muscularis and the mucosa in only a
few places. Its origin was without doubt in the submucosa.
Sections of the smaller tumor showed the same structure met
with in the larger. No trace of lymphatic tissue, however, re-

mained. There was markedly little inflammatory reaction about and in the tumors of the stomach; no groups of tumor cells were found in either blood or lymph vessels. Some of the veins, however, contained recent thrombi.

Sections of the small tumor situated in the submucosa of the duodenum showed a typical adenoma, composed of a large number of glands divided into lobules by connective tissue bands. The glands were lined with a single row of epithelial cells, which were columnar in some and cuboidal in other glands. The cytoplasm of these cells was finely granular and stained poorly; the nuclei were vesicular and placed at the base of the cells, where the latter were supported by a delicate membrana propria. The epithelial cells formed a single row in the glands and never broke through the membrana propria. No ducts were to be found. The tumor lay almost entirely in the submucosa, but in some places had pushed through the muscularis mucosæ and encroached upon the mucosa, which was normal in appearance. Sections of the tumor of the thyroid showed a papillary adenoma. The other organs are without present interest.

Case 3.—Sarcoma of the pylorus. G. H., white, a laborer, aged 48 years, was admitted to St. Alexis' Hospital, service of Dr. Cogan, Oct. 26, 1900, complaining of vomiting and weakness. His family history was negative. The patient stated that he had always enjoyed good health until December, 1899, when his appetite failed and he began to lose weight. In October, 1900, he had to give up work on account of weakness and discomfort in his stomach. At this time he began to vomit after each meal. After admission to the hospital he vomited almost continuously until his death, which occurred on November 3. No food could be retained by the stomach.

Examination of the chest was negative. No tumor could be felt in the abdomen. On testing the stomach contents the acidity was normal. Motility and absorption were both diminished. The red blood cells numbered 1,000,000 per cubic millimeter. The leucocytes were not increased.

*Anatomic Diagnosis:* Sarcoma of the pylorus and neighboring portion of the stomach. Broncho-pneumonia of both lungs. Chronic adhesive pleuritis. Anemia.

The body was poorly nourished. Rigor mortis was present. The other organs showed nothing of present interest; only the description of the stomach is taken from the autopsy protocol.

*Stomach:* This was somewhat dilated. On opening the organ the pylorus and the wall of the stomach on all sides for a distance of 10 cm. from the pylorus, were found to be thickened. The mucosa was unbroken. The gastric wall at the pylorus measured from 1 to 2 cm. in thickness. The tumor on section was at nearly every point beneath the mucosa, and its chief

seat was the submucosa, but in many places it could be traced into the muscularis. The tumor was homogeneous in appearance and firm in consistency. The lymph glands in the neighborhood of the stomach were not enlarged. No metastases were found in any organ.

In sections made from various portions of the tumor the mucosa was atrophied, the tubules having been compressed and the interglandular stroma replaced by fibrous tissue containing, round, oval or fusiform cells. The muscularis mucosæ was absent in many places. The submucosa was everywhere thickened, due to a new growth of fibrous tissue, containing a varying number of fusiform, round and oval cells, supported by a variable amount of intercellular substance. At many places this tissue extended into the muscularis. In some places the sarcomatous tissue was markedly fibrous. Throughout the tumor the capillaries were numerous. In many places the lymph vessels were dilated and contained tumor cells. In some places the endothelial cells of the lymphatics showed marked proliferation and nearly filled the lumina of these vessels. In some lymphatics the lining cells had assumed a cuboidal shape and the structure had the appearance of a tubular gland. The new growth in some places invaded the nerves and even the serosa. There was no peritonitis.

CASE 4.—A saloonkeeper, aged 39 years, married and a moderate drinker, suffered with occasional attacks of indigestion and discomfort in the epigastrium for a year before consulting Dr. Robert H. Sunkle, to whose kindness I am indebted for the history and autopsy in this case. When first seen by Dr. Sunkle, the man complained of pain in the abdomen, loss of weight, strength and appetite. The liver was greatly and uniformly enlarged, but no nodules were palpated. No tumor could be made out in connection with the stomach. The heart and lungs were negative. There was occasional vomiting, but no special pain referable to the stomach.

A few days before death, which occurred one month after Dr. Sunkle first saw the case, dulness was made out in the flanks. Dr. Sunkle's diagnosis was hypertrophic cirrhosis of the liver, in which he was upheld by Dr. Sihler, who saw the case in consultation. Later the possibility of carcinoma of the liver was considered.

The autopsy was made by Dr. Sunkle, who brought the organs to my laboratory for examination.

*Anatomic Diagnosis:* Primary angio-sarcoma of the lesser curvature of the stomach, with metastases in the neighboring lymph glands and in the liver.

As the stomach and liver were the only organs showing changes of present interest, a description of the other organs is omitted.

*Stomach:* The organ was of ordinary size. The lesser curvature was thickened. On section, the cardiac and pyloric ends were normal, as were the greater curvature and the anterior and posterior walls. The mucosa was somewhat thickened. The whole length of the lesser curvature was thickened and from it a mass of tissue protruded into the cavity of the organ. The mass was from 1.5 to 2 cm. in thickness and 4x5 cm. in outline. The surface was irregularly ulcerated and it was difficult to make out the mucosa. On section the tumor was soft, readily broken down, and lacked the pearly translucency of carcinoma. The growth extended through the coats of the stomach, and included and surrounded several enlarged lymph glands, which were virtually involved in the growth. On section these glands were soft and had the same appearance as the gastric tumor.

The peritoneal cavity contained a large amount of clear fluid. There was no peritonitis. The liver was markedly enlarged, its edges rounded, the capsule mottled red and yellow. Scattered over the surface, but lying well beneath the capsule, there were a number of soft yellowish areas. On section both the right and left lobes of the organ were the seat of numerous grayish-yellow areas of soft consistency, sharply marked off from the surrounding liver tissue, and varying from 0.5 to 3 or 4 cm. in diameter. Many of the large branches of the portal vein were occluded by grayish-yellow masses, which were here and there mixed with blood and coagula. Portal vessels could be traced into many of the larger masses, which often contained central hemorrhagic areas. The liver tissue between the masses was congested and in places compressed. The external surface of the gall bladder showed a small nodule similar to those found in the liver. The gall bladder and bile ducts on section were normal. The mesenteric glands and other organs were free from metastases.

*Histologic Examination:* Stomach. In sections of the gastric wall made at a distance from the tumor, there was disintegration of the superficial layer of the mucosa. In sections cut through the tumor at various places the mucosa showed disintegration to a varying depth. In some sections the deeper layers of the mucosa were invaded by tumor tissue which compressed and replaced the tubules and interglandular tissue. The submucosa was markedly thickened, due to the presence of large areas of tumor tissue which was diffuse in some places and in others sharply circumscribed. This latter appearance was usually due to the extension of tumor tissue into large and small veins. The tumor evidently had its origin in the submucosa and varied in structure considerably. In many places the structure was typical of a mixed cell sarcoma, being composed of large and small round and oval cells, large spindle-shaped and numerous giant cells, and a variable 'amount of

intercellular tissue, which was conspicuous in some places and scanty in others. In general, the tumor was very cellular. In all parts of the growth, capillaries, most of which contained blood, were numerous. In most places the relation of the tumor cells to the capillaries was intimate, viz., masses of round, oval, flattened and often fusiform cells surrounded blood capillaries, and were placed directly in relation with their walls. In some places, especially in the metastases in the liver, tumor cells were arranged in a regular row about a small lumen, in such a manner as to resemble a cross-section of a tubule. Blood cells and granular material were present in some of these spaces. In still other places the tumor cells were arranged in large alveoli, supported by a variable amount of intercellular tissue and capillaries. The muscularis was only slightly invaded, and the mucosa was markedly invaded in places. The invasion of the large and small veins of the submucosa was marked. Most of these vessels in the tumor area were completely occluded by tumor tissue, similar to that above described. The tumor cells varied much in size and shape. Their nuclei were large, round or oval, some staining densely, while in others fine chromatin masses could be made out. In many nuclei there was a rather large oval or round hyaline body, which stained pink with eosin. Nuclear figures were common. The giant cells had very large single nuclei. Many of the tumor cells showed marked fatty degeneration. The growths in the lymph glands and the liver were identical with that of the stomach. The relation of the tumor cells to the capillaries was especially well marked in the liver metastases. Some of the branches of the portal vein contained both tumor cells and fibrinous thrombi. Many were completely occluded. In many places the new growth in the liver had passed through the veins and was infiltrating the liver tissue. In sections some distance from metastases, there was marked necrosis of the central portions of the liver lobules with hemorrhage. There could be no doubt in regard to the sarcomatous nature of the neoplasm, which evidently sprung from the blood vessels of the submucosa of the stomach.

*Frequency.*—The disease is certainly rare, but probably occurs more commonly than is generally supposed. There can be no doubt but that in the absence of routine microscopic examination of tumors found at operation and autopsy, many cases must have been mistaken for carcinoma, which, indeed, was the clinical diagnosis in a considerable number of the recorded cases. So far there are sixty-one known cases. Next to carcinoma it is certainly the most common tumor of the stomach.

*Etiology.*—Of the 61 cases 30 occurred in females, 25 in males and in 6 the sex was not mentioned. In regard to age the youngest reported case occurred in a girl 3½ years old (Findlayson's, lympho-sarcoma). The age was reported in 52 cases and the ages were as follows: It was from 15 to 20 years in 6 cases; 20 to 30 in 9 cases; 30 to 40 in 7 cases; 40 to 50 in 10 cases; 50 to 60 in 10 cases; 60 to 70 in 5 cases; 78 in 2 cases, and given as "old age" in 2 cases. Nothing is known of the primary cause of the disease. In Brooks' case the tumor started in an old bullet wound of the stomach.

*Seats of Tumors.*—Heretofore on account of the meager data at hand little attempt has been made to establish the principal seats of sarcoma of the stomach. Schlesinger and Dock concluded that any portion of the gastric wall might be affected. The former states that the greater curvature is the most common seat, especially of the nodular form, while lympho-sarcomata are apt to be diffuse. Dock calls attention to their origin at the pylorus and in the posterior wall in some of the recently reported cases.

Analysis of the 61 cases shows that the growth was diffuse in 13, of which 4 were lympho, 5 round cell, 1 fibro and 1 spindle-cell sarcoma. In 8 cases the growth was limited to the pylorus, in 6 cases the pylorus and the lower half of the stomach were involved, in 1 the pylorus and the upper part of the duodenum, and in 1 the pylorus and the greater curvature; the pylorus was involved in a total of 16 cases. The tumors were primary in the greater curvature in 7 cases, and involved the greater curvature with the posterior wall in 1 case, with the lesser curvature and posterior wall in 2 cases, and with the anterior wall in 1 case, making the total involvement of the greater curvature 11 cases. The lesser curvature alone was involved in 5 cases, with the cardia in 3 cases, with the posterior wall in 1 case and with the posterior wall and greater curvature in 1 case. The posterior wall alone was affected in 6 cases, and with the anterior wall in 1 case. The cardia was involved in only 3 cases, and always with the lesser curvature. The anterior wall was never involved alone, but was affected with the posterior wall in 1 case, and the greater curvature in another.

It is seen from the above that the growth involved

the pyloric end in a total of 16 cases, the cardiac end in 3
cases, the intermediate portions in 27, while it was said
to be diffuse in 13 cases. The seat of the growth was not
mentioned in 5 cases. The stomach and whole gastro-
intestinal track were involved in 1 case of lympho-
sarcoma.

Pyloric stenosis was noted in only 5 cases, but prob-
ably occurred more frequently, for the reports are mea-
ger in many instances.

*Size of Tumors.*—They were stated to have been the
size of a pigeon's egg in 1 case, a man's fist in 2 cases,
an orange in 1 case, a child's head in 5 cases, and a
man's head in 6 cases. The tumors extended below the
umbilicus in 8 cases.

*General Appearances.*—They were said to have been
nodular in 27 instances, and in some of these, notably
in 2 cases, the tumors formed polypoid masses project-
ing into the lumen of the stomach. Tumors projected
into the peritoneal cavity in 8 cases. In some of the lat-
ter cases the base of the tumor was narrow. The new
growths showed ulceration in 10 cases, with perforation
of the gastric wall in 2 cases.

In many instances, the exact number of which could
not be determined, the growth developed beneath the
mucosa, which was intact. The growth usually started
in the submucosa, and the muscularis was commonly in-
volved. The tumors occasionally had their origin in the
muscularis, and cases of myosarcoma are recorded.

The tumors varied much in consistency, from soft,
spongy, fungoid masses to firm, fibrous growths, and had
the general macroscopic characters of sarcoma of other
organs. They differed from carcinoma in their
situation, being usually beneath the mucosa and
often not involving the latter, and also in their nodular
character, comparative dryness and homogeneous ap-
pearance on section. In many cases the diagnosis was
not made until microscopic examination. This was, no
doubt, often due to lack of care in the macroscopic exam-
ination. Cystic degeneration of the tumors occurred in
6 cases, hyaline degeneration in 1, calcification in 3,
myxomatous degeneration in 2, and suppuration in 1.
The stomach is stated to have been decreased in size in 2
cases, and in 1 case, the second reported in this paper, it
was constricted in the middle and resembled an hour

glass in shape. In a few cases, dilatation of the stomach is mentioned, but this seems to be much less common and not so marked as in carcinoma. It will be noted that the pyloric end of the stomach was involved in only 16 out of 61 cases—26.23 per cent.—and that pyloric stenosis was noted in only 5 cases—8.19 per cent. The stomach was bound to the right lobe of the liver in one case and to the spleen in another.

*Involvement of Other Glands.*—Metastases occurred in 24 cases—40 per cent.—a smaller proportion than in carcinoma. The gastro-hepatic lymph glands were involved alone in 2 and with other organs in 5 cases; the mesenteric glands in 6 cases, never alone; the retroperitoneal glands alone in 1 case and with other organs in another. The omentum was invaded in 2 cases, the liver in only 7 cases, the spleen in 4, the kidneys in 2, the ovaries in 3, the peritoneum in 2, and the intestines, pancreas, thyroid, right adrenal, and testis each in 1 case. In our Case 4 there was extensive sarcomatous embolism of the branches of the portal vein, with multiple large metatases of the liver.

*Histologic Classification.*—The growths were classified as round cell in 16 cases, spindle cell in 8, mixed cell in 4, as lympho-sarcoma in 15, myosarcoma in 4, fibro-sarcoma in 3, angio-sarcoma in 3, and endothelial (lymph) sarcoma in 1. The histologic diagnosis was not given in 7 cases. In Case 4 of our series giant cells were numerous.

*Clinical Symptoms.*—Reigel states that there is no clinical difference between sarcoma and carcinoma of the stomach, and that hematemesis and cachexia are common to both. Schlesinger found that examination of the stomach contents (7 cases reported by Hammerschlag, Maass, Dreger, Fleiner and Schlesinger) showed nothing essentially different from that of gastric carcinoma. Dock, who has presented the most carefully studied case, made a diagnosis of dilatation from a tumor at the pylorus, probably the scar of an old ulcer, but also thought of carcinoma and sarcoma, "but the features of the case were not considered to admit a differential diagnosis."

According to Reigel the clinical course runs from a few months to three years, on an average of from 1 to 1½ years. In several cases death occurred within from

four to six months from the onset of nausea and vomiting and epigastric pain. Many cases run their course without symptoms until near the end. Case 4 illustrates this point. In some cases there were no clinical symptoms referable to the stomach. In Hartley's case there was coffee-ground vomit and dyspepsia five years before the case came under observation. There was no recurrence and except for symptoms of indigestion, fair health was enjoyed for four years, when coffee-like material was vomited on five successive mornings.

Analysis of the cases shows that the duration of the illness was mentioned in only 16 cases as follows: Six weeks, 1 case; 3 months, 1 case; 5 months, 1 case; 7 months, 1 case; 9 months, 1 case; 1 year, 4 cases; 2 years, 1 case; 3 years, 1 case; several years, 1 case; 5 years, 1 case. Vomiting was recorded in 18 cases, in 4 of which the vomitus was bloody. Loss of appetite was recorded in 5 cases, but was probably a common symptom. Diarrhea was a marked symptom in 2 cases, but constipation seems to have been of frequent occurrence. Pain in the gastric region was complained of in 6 cases; pain in the abdomen was noted in 9 cases, in 3 of which it dated for 2 years.

Tumors were palpated in the gastric region in 10 cases, in the splenic region in 6, and in the lower abdomen in 13 cases. In Case 4 the liver was enormously enlarged with no symptoms suggestive of disease of the stomach. Emaciation was noted in 13 cases.

The condition was mistaken for pseudo-leukemia in 1 case, and for pernicious anemia in 1 case; ascites occurred once and jaundice twice. Dock found that the blood in the cases of gastric sarcoma previously reported showed a decrease in the hemoglobin and in the number of red blood cells, and usually leucocytosis.

*Diagnosis.*—A diagnosis was either not made or not mentioned in 38 cases. In 5 cases a diagnosis of gastric carcinoma is recorded; in 8 cases the diagnosis was "malignant tumor" of the stomach, while a positive diagnosis of sarcoma of the stomach was made in 3 cases, one each by Schlesinger, Reigel and Westphalen. In the latter's case the diagnosis was made on the microscopic appearances of a bit of tissue obtained on washing the stomach. In Reigel's case a large sarcomatous nodule was vomited. A probable diagnosis of an old scar of the

pylorus was made in one case by Dock. The diagnosis
was tumor of the spleen, tumor of the omentum, tumor
of the left hypochondrium, cystic tumor of the abdomen,
ovarian cyst and pseudo-leukemia, each in one case. In
Case 4 the diagnosis was hypertrophic cirrhosis of the
liver. Little mention is made of differential diagnosis in
the literature, and Dock undoubtedly states the case cor-
rectly when he says, that so far as the earlier stages are
concerned we have no specific symptoms of sarcoma of the
stomach and even when a tumor is present (palpable)
it can not be differentiated from cancer (carcinoma). As
previously pointed out, analysis of the gastric contents
has hitherto been of no aid in differential diagnosis be-
tween gastric sarcoma and carcinoma.

Analysis of the 61 cases at our disposal brings out
several points which may be of assistance in a differen-
tial diagnosis between sarcoma and carcinoma after the
presence of a gastric tumor is established. In the first
place age has an important bearing. It was shown to
be as follows: One case of lympho-sarcoma of the stom-
ach occurred in a girl 3½ years old; 7 were below 20
years; 23, or 37.7 per cent., were below 40, and only
one-third of the cases occurred between 40 and 60 years,
the most common period for the occurrence of carci-
noma of the stomach.

In 16 cases, or 26.23 per cent., the tumors were situ-
ated at the pyloric end, causing pyloric stenosis in only
5 cases. In but 3 cases was the cardia involved. In the
other 41 cases the tumors were seated between the py-
lorus and cardia, without involving either. These facts
are not, however, of as much assistance as they seem at
first glance, for it is chiefly in the cases in which the
ends of the organ are involved, that symptoms of gastric
tumor occur. The growth was diffused over the surface
of the organ in 13 cases. Accurate figures could not be
obtained, but it is clear from reading the reports of the
recorded cases that dilatation of the stomach is much
less common in sarcoma than in carcinoma of the stom-
ach. In several cases the stomach was decreased in size.
Gastric sarcoma was mistaken for tumor of the spleen
or splenic region in 3 cases, and this is very natural in
a case of large tumor mass of the greater curvature with-
out gastric symptoms; see our Case 2.

The size of the tumor is a point of considerable diag-

nostic importance. In 6 cases the tumor was the size of a man's and in 5 of a child's head; in 3 cases they weighed from 10 to 12 pounds, projecting into the peritoneal cavity in 8 cases, and below the umbilicus in 9 cases. One case was operated on for tumor of the omentum, and another for ovarian cyst.

Although many cases run a short course, in a few instances gastric symptoms extended over a period of from two to five years. As previously pointed out, many cases run their course without symptoms until near the end, and frequently there are no symptoms referable to the stomach. The appetite and the gastric functions may continue to the end.

*Treatment.*—It is of interest to know that eleven cases have been operated on, with four deaths. In one case, that of Mintz', the patient recovered from a gastro-enterostomy, but died later from the tumor. A portion of the tumor was excised in two cases—Baldy and Dreger. In one case pus was evacuated from a gastric sarcoma with a fatal termination. In six cases the tumors were removed. In Capello's case, a woman 54 years old, a large cystic sarcoma of the stomach, the size of a man's head, mistaken for an ovarian cyst, was successfully removed. The patient was in good health two years later. In a woman 52 years of age, Cantwell found a spindle cell sarcoma weighing 12 pounds, growing from the posterior wall of the stomach over a surface of five inches square. The tumor was successfully removed, but a secondary growth was discovered six months later. A successful operation for the removal of sarcoma of the stomach is credited to Billroth. In Dock's case, a man of 55 years, Nancrede successfully removed about one-third the long axis of the stomach and 2 cm. of the duodenum for a lympho-sarcoma, measuring 6 by 4 cm. The patient was well and had gained thirty pounds two months later. Hartley's case was even more remarkable. A woman 54 years of age, five years before coming under observation, vomited coffee-ground-like material, but had no other symptoms. There was no recurrence, and for four years she was in fair health, except for symptoms of indigestion which did not interfere with work. A year before applying for treatment she vomited coffee-ground-like material for five successive mornings. Pain in the back was a marked symp-

tom. On physical examination a large, hard, elastic tumor was felt in the left lumbar and umbilical regions. At operation a large pedunculated tumor was removed from the posterior wall of the stomach. Schapf resected the entire stomach, the seat of a large lympho-sarcoma, in a woman, who gained flesh and was apparently well one year after operation.

*Conclusions.*—1. Gastric sarcoma is more common than is generally supposed, at least 61 cases being recorded. Careful routine microscopic examination of all gastric tumors met with at autopsy and operation will probably show a marked increase in the occurrence of these tumors. 2. The two sexes are affected in about equal proportions, as against five males to four females for carcinoma; 37.7 per cent. of the cases occurred below the fortieth year, and 11.44 per cent. (7 cases) below the twentieth year. 3. The pyloric end was involved in only 26.23 per cent. of the cases, as against 60 per cent. for carcinoma (Welch), and caused stenosis in only 8.19 per cent. of the entire number of cases. Diffuse growths occurred in 21.31 per cent., while the cardia was involved in only 4.9 per cent. The posterior wall and greater curvature are commonly involved. 4. Gastric sarcoma may reach a large size, that of a child's or man's head, and may project as large masses into the lumen of the stomach or into the peritoneal cavity, extending below the umbilicus—13.1 per cent. Such tumors have been mistaken for tumors of the spleen, omentum and ovaries, and may be pedunculated and readily removed. 5. Gastric sarcomata commonly start in the submucosa or muscularis and are less apt to ulcerate and cause hemorrhage than carcinomata. 6. All the histologic varieties of sarcoma have been found in the stomach. 7. While most of the cases in which the duration of the illness was mentioned ran an acute course, the average duration of life is probably from nine to ten months, while in one case it was three and in another five years. 8. Metastasis is not as frequent as in carcinoma, but may be widespread. The liver was invaded in only seven cases—11.47 per cent.—in striking contrast to gastric carcinoma, which, according to Welch's statistics, invaded this organ in 30 per cent. of cases. 9. There are no distinctive clinical symptoms or physical signs of sarcoma of the stomach, but a positive diagnosis has

been made in three cases from microscopic examination of material obtained from the stomach. 10. In cases of large tumors connected with the stomach, especially when they project to or below the umbilicus, a diagnosis of sarcoma of the stomach is warranted. A tumor of the stomach in an individual under 20 years of age is almost certainly sarcoma. In our series 37.7 per cent. of the cases were under 40, while in Osler's 150 cases of carcinoma of the stomach only 15.3 per cent. were under this age. 11. Operation should be as successful in sarcoma as in carcinoma of the stomach.

### BIBLIOGRAPHY.

Chapman: Am. Jour. Med. Sc., 1877, vol. lxxiv, p. 433.
Targett: Trans. Path. Soc., London, 1889, vol. xl, p. 76.
Stephan: Jahrbuch f. Kinderheilk., 1890, Bd. 30, s. 354.
Shaw: Trans. Path. Soc., London, 1891, vol. xlii, p. 90.
Rolleston: Ibid., 1893, vol. xliv, p. 65.
Albrecht: Wiener Med. Presse, 1895, No. 17.
Ogle: Ibid., 1896, vol. xlvii, p. 40.
Livingood: Bull. Johns Hopkins Hosp., 1898, vol. ix.
Gastpar: Centralbl. f. Allgem. Path. und Path. Anat., 1900, Bd. xl, s. 81.
Stark: Virchow's Archiv, 1900, Bd. 162, s. 256.
Perry and Shaw: Guy's Hosp. Rep., 1892, p. 147.
Bruch: Diag. d. bösartigen Geschw., Mainz, 1847. Quoted by Schlesinger.
Virchow: Die Krankh. Geschülste. 1864-65.
Cayley: Trans. Path. Soc., London. 1869, vol. xx, p. 170.
Kosinski: Virchow-Hirsch's Jahresbericht, 1875, ii, s. 226.
Brodowski: Virchow's Archiv., 1876, Bd. 67, s. 227.
Wickham Legg: St. Bartholomew's Hosp. Rep., 1874, vol. x.
Coupland: Trans. Path. Soc., Lond., 1877, No. xx, p. 170.
Hardy: Gazette des Hôpitaux, 1878, No. 4, p. 25.
Jungman: Inaug. Dissert., Würzburg, 1882.
Weissblum: Inaug. Dissert., Griefswald, 1886.
Billroth: Wiener Med. Presse, 1888, Nos. 4 and 5.
Salzer: Wiener Med. Wochensch., 1888, No. 2, s. 38.
Malvoz: Annal. Soc. Medico-Chirur. de Liege, 1890, Nos. 8 et 9, p. 339. Quoted by Tilger.
Zahn: Quoted by Krüger, but reference not found.
Perry and Shaw: Guy's Hospital Reports, 1892, vol. xlviii, p. 147.
Von Hacker: Chirurg. Beit. a. d. Erzhorzogen Sophien-Spital in Wien, 1892. Quoted by Krüger.
Von Török: Lympho-sarcoma der Magen-wand. Centralbl. f. Chirur. Quoted by Schlesinger and others, but was not found in the above issue.
Tilger: Virchow's Archiv, 1893, Bd. 133, s. 181.
Westphalen: St. Petersb. Med. Wochensch., 1893, p. 403.
Kundrat: Wiener Klin. Woch., 1893. Quoted by Schlesinger. Ref. not found in this journal.
Krüger: Inaug. Diss., Berlin, 1894.
Rasch: Hospitaltidende, 1894, s. 849. Quoted by Schlesinger.
Redtenbacher: Jahrb. der Wien. Krankenst., 1894, s. 560.
Drost: Inaug. Diss., München, 1894.
Dreyer: Inaug. Diss., Göttingen, 1894.

Hammerschlag: Untersuch. ü. d. Magen Carcinoma. Beob. Archiv, f. Verd. Krankh., Bd. ii, Heft 1.

Ewald: Klinik der Verdauungskr., 2 Th., s. 354, 3d Aufl.

Fliener: Lehrb. d. Krankh. d. Verdauungs-Organe, 1 Th., s. 295, u. 311.

Moass: Deuts. Med. Wochensch. (Vereinsb.), 1895, s. 34.

Kosinski: Centralbl. f. Chirur., 1895, s. 796.

Hanseman: Natùrforscherv, s. Lüberck, 1895. Quoted by Schlesinger.

Hartley: Ann. of Surg., 1896, vol. i, p. 609.

Weiss: Jahrb. d. Wiener Krankenanst., 1896, Bd. iii.

Stendel: Brun's Beiträge, Case 7, Bd. 23, s. 1.

Heyem et Lion: Traité de Médicine et de Therap., 1897, T. iv.

Schlesinger: Zeitsch. f. Klin. Med., Bd. 32, Supplement-heft, 1897.

Kehr: V. Langenbech's Archiv, Bd. 58.

Lindner und Kuttner: Die Chirurg. d. Magens und ihre Indicat., 1898, s. 261.

Robert: Allegem. Med. Centralztg., 1898, No. 94, s. 1153.

Baldy: THE JOURNAL A. M. A., 1898, i, p. 523.

Brooks: Medical News, 1898, i, p. 617.

Cantwell: Annals of Surgery, No. 5, 1899.

Capello: Centralbl. f. Chirurgie, 1899, No. 20, s. 609.

Schopf: Ibid., No. 43, s. 1163.

Finlayson: Brit. Med. Journal. 1899, 2, p. 1535.

Reigel: Die Erkrank. des Magens, ii Theil., p. 847. Nothnagel's Spec. Path. und Therapie. Bd. xvi, Th. ii.

Dock: Trans. Assn. Am. Physicians, 1900.

Mintz: Berliner Klin. Wochensch., 1900.

## THE ORIGIN OF GAS AND GAS CYSTS OF THE CENTRAL NERVOUS SYSTEM.

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*I. The Occurrence of Gas in the Cerebral Vessels without Gas Cysts of the Brain.*

*Case I.** — The body of a male, who died in Lakeside Hospital of lung tuberculosis, and on which the autopsy was performed six hours after death, showed gas bubbles in the heart, liver, spleen, and kidneys, in the portal, splenic, and renal veins, as well as in the cerebral sinuses and the blood vessels of the dura and pia arachnoid, with the presence of B. aërogenes capsulatus in pure culture. No gas cysts were present in the brain tissue.

*Case II.* — Summary. General gaseous emphysema of the subcutaneous tissues, the brain and lungs, gas bubbles in the heart, aorta, cerebral, renal, hepatic, and splenic veins, associated with the presence of B. aërogenes capsulatus and B. mucosus capsulatus.

On May 16, 1900, I performed an autopsy on a newborn child which had remained in a privy vault for three days during very warm weather. The following is abstracted from the autopsy protocol:

The body is of ordinary length, and is free from scars and wounds. No bones are broken. The face is bloated; the skin of the scalp, trunk, and lower limbs is of a dark bluish hue. A portion of the umbilical cord, which is not tied, and which is of a grayish color on section, projects from the umbilicus. The cord contains no pus. On both forearms there

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* This is Case XIII. of my article "A Contribution to the Knowledge of B. aërogenes capsulatus," Contributions to the Science of Medicine, dedicated to Wm. H. Welch, Baltimore, 1900.

are several large blebs containing clear fluid. The subcu-
taneous tissues of the scalp, trunk, and extremities crackle
on pressure and show marked gaseous emphysema on
section.

The abdomen is distended and on section collapses with
the escape of gas.

The chest is well formed, the ribs and costal cartilages and
sternum are normal. The thymus is well developed. The
precordial space uncovered by the lungs is of ordinary size.
The anterior border of the upper lobes are from one to two
centimetres apart. The pleural cavities are free from fluid
The pleuræ are smooth. Beneath the pleuræ over all the
lobes of both lungs there are a large number of emphysema-
tous areas varying in size from a pin's point to that of a split
pea. The lungs on section present the same general appear-
ances. They are of a pinkish white color, with here and
there small darker areas. They are free from consolidation,
crepitate and float in water. The bronchi are normal. The
larger pulmonary vessels contain gas. The bronchial and
other glands, with the larynx and trachea, and structures of
the mouth are negative.

The pericardium is normal and free from gas. The heart
is of ordinary size; the valves are normal. The musculature
is of a pale pinkish gray hue, and contains numerous gas
bubbles, as do the vessels. The aorta and large veins, especi-
ally the veins of the neck, contain numerous gas bubbles.

The liver, spleen, and kidneys are dark red in color, soft,
and show advanced decomposition. The vessels of all three
organs on section contain numerous gas bubbles.

The œsophagus, stomach, and intestines are distended with
gas, are of a bluish green color, and contain a soft, yellowish
material.

The sexual organs, which are those of a female child, are
normal. The pancreas, suprarenal capsules, and lymph
glands appear normal. The bladder is distended with gas.

Head. — On section the scalp is found to be raised from the
bone and markedly emphysematous. The bones of the skull
and the fontanelles˙ are normal. The dura mater is con-

gested. The brain tissue is disintegrated into a pulpy mass of a pinkish gray color containing large numbers of gas bubbles. None of the brain structures can be recognized, the whole being transformed into a semifluid mass. The vessels at the base of the skull appear normal. The sinuses and the larger veins contain gas bubbles.

*Bacteriological Examination.* — Coverslip preparations were made from the various organs, brain, heart's blood, lungs, liver, spleen, kidneys, and subcutaneous tissues. In the brain, lungs, and subcutaneous tissues there were large numbers of short and long, stout encapsulated bacilli, staining by Gram's method, and having the morphology of B. aërogenes capsulatus. In addition to this organism there were variable numbers of thinner bacilli, and oval and coccal forms, suggestive of B. mucosus capsulatus. Both forms were scanty in the liver and kidneys.

Anaërobic glucose agar Petri-plate cultures from the brain, lungs, heart, liver, and kidneys gave an abundant growth of two kinds of organisms, which on further study proved to be B. aërogenes capsulatus, and a pleomorphic bacillus of the B. mucosus capsulatus group. The latter organism was pathogenic for guinea-pigs. A rabbit inoculated in the ear-vein with a bouillon-suspension of the gas containing and disintegrated brain and killed soon afterwards, showed general gaseous emphysema with both large and small capsulated bacilli. Anaërobic cultures showed both B. aërogenes capsulatus and B. mucosus capsulatus. The former would not grow aërobically, while the latter grew aërobically and anaërobically.

Glucose agar Petri-plate cultures grown aërobically from the various organs at the autopsy gave a bacillus of the B. mucosus capsulatus group identical with the one obtained in the anaërobic cultures.

There were found, then, in the various organs of this case both B. aërogenes capsulatus and B. mucosus capsulatus.

Sections of the lungs showed atalectasis everywhere, the walls of the air vesicles being in juxtaposition. Some of the small bronchi were distended, the epithelial cells lining them

being flattened. Here and there in the lung tissue there were empty holes or spaces. These sometimes represented dilatations of the air vesicles, but were often seated in the interstitial tissue; many of them were subpleural. Large bacilli were present in the bronchi and in the gas holes.

Sections of the liver, spleen, and kidneys showed typical gas cavities, containing bacilli. Two varieties of bacilli were found, large stout bacilli resembling B. aërogenes capsulatus, and thinner pleomorphic bacilli suggestive of B. mucosus capsulatus.

Anatomical Diagnosis. Still birth. General gaseous emphysema of the subcutaneous tissues, the brain and lungs, with gas bubbles in the heart, aorta, and the cerebral, cervical, renal, hepatic, and splenic veins, and in the urinary bladder; associated with the presence of B. aërogenes capsulatus and B. mucosus capsulatus.

The explanation of the absence of gas cysts of the brain in these cases is plain. In the first case the time elapsed between death and the autopsy was insufficient for gas cysts to form in the brain, while in the second case, although gas was present in the brain, the latter had undergone disintegration before the autopsy was made. In the second case the bacilli probably entered the body by both the alimentary and the respiratory tracts. Both the varieties of bacteria present in this case are probably commonly present in privy vaults. Harris[1] isolated B. aërogenes capsulatus from a cesspool, while I have found it frequently in the intestinal contents. As is well known, B. mucosus capsulatus is also commonly present in the latter. The association of B. aërogenes capsulatus and B. mucosus capsulatus in gaseous emphysema is of considerable interest, for Perkins[2] and I[4] have both found the latter organism the sole cause of gas formation in post-mortem gaseous emphysema.

Case II. shows the fallacy of the "floating" test for ascertaining at autopsy whether a newborn child has breathed, for in this case bits of the lung floated on water (on account of the gaseous emphysema present), while microscopical examination showed the alveolar walls in juxtaposition.

*II.  Gas Cysts of the Central Nervous System.*

The first description of gas cysts of the central nervous system were those of Reuling and Herring and of the writer published in the same journal in April, 1899.[3]

Reuling and Herring found in the brain of a woman who died three days after an operation for gun-shot wound of the intestines, a cavity 5 X 1 X 2 cm. in the external capsule, and a number of smaller cavities in the internal capsule, the optic thalmus and external orbital convolutions of the right cerebral hemisphere; and similar small cavities in the left external capsule and lenticular nucleus, as well as in the cerebellum.  There were no inflammatory lesions of the brain or its membranes.  The other organs were free from gas. As the cavities were not discovered until after the brain was hardened in formalin, cultures were not made.

Microscopically the cavities were smooth and without a lining membrane.  Some were surrounded by comparatively normal brain tissue, while about others there was " an area of cell degeneration of variable thickness," which stained diffusely with eosin; outside of this there was a zone in which there was a partial loss of nuclear staining.  The cavities were empty except for masses of bacilli, which were distributed chiefly along their margins.  Some bacilli filled the majority of the capillaries and were apparently present in pure culture.  The bacilli had the morphological and staining characters of B. aërogenes capsulatus, with which they were thought to be (and doubtless were) identical.

The bacilli were also found free in the tissue, surrounded by areas of cellular degeneration, and areas of the latter were sometimes seen about blood vessels containing bacilli. There was no evidence that the lymphatics played any part in the process.

*Case III.* — In my case [3], [4] there were acute fibrino-purulent cerebro-spinal meningitis and ependymitis with multiple cerebral abscesses, gas cysts of the cerebro-spinal membranes, of the exudation, of the cerebrum, and of the liver; with gas bubbles in the sinuses and meningeal vessels, in the heart, liver, spleen, kidneys, and peritoneal cavity, oc-

curring in a man who died seven days after an operation for
the cure of an urethro-perineal fistula. B. aërogenes cap-
sulatus was found in pure culture and large numbers in the
various lesions. For full descriptions with illustrations of the
lesions the reader is referred to my previous article. (L. C.)

Gas cysts occurred about the abscesses of the brain and in
the lenticular nuclei.

On histological examination the gas cysts of the exudate
as well as those of the membranes and brain contained large
bacilli. The cysts of the brain tissue showed simply separa-
tion and compression of the tissues. There was absence of a
lining membrane and inflammatory reaction. None of the
cysts appeared to be due to dilatation of the blood vessels,
and most of the latter did not contain bacilli. The gas for-
mation probably occurred after death.

*Case IV.* — In a second case, in which the infection atrium
was a gastric ulcer, I[5] found gas cysts of the brain with gen-
eral gaseous emphysema of the subcutaneous tissues, the
heart, blood vessels, liver, spleen, kidneys, and stomach, with
bacteriatemia due to B. mucosus capsulatus. B. aërogenes
capsulatus was carefully excluded, by examination of cover-
slip preparations, sections of hardened organs, by aërobic
and anaërobic cultures and animal experiments. Gas bub-
bles occurred in all the cerebral vessels and in the pia-
arachnoid. There were no inflammatory changes. The
internal capsules and lenticular nuclei contained numerous
round and oval smooth walled cysts, varying from one to
twelve millimetres in diameter.

Histological examination showed cavities without a lining
membrane, due to separation and compression of the brain
tissue without necrosis or disintegration. The blood vessels
and cysts contained large numbers of small pleomorphic
bacilli of the size and appearance of B. mucosus capsulatus.

*Case V.* — Summary. Multiple gas cysts of the cerebrum
and cerebellum of a human cadaver, due to bacilli morpho-
ogically identical with B. aërogenes capsulatus.

The brain of this case was removed from a cadaver in the
dissecting room of the Western Reserve Medical College;

and hardened into formalin before section.   Nothing is known
of the clinical history or anatomical findings, and no case of
general gaseous emphysema of the cadaver has been observed
in this dissecting room.   I owe the opportunity of studying
this brain to the kindness of my colleague, Prof. C. A.
Hamann.   Nothing unusual was noticed upon the surface of
the brain, which was given to a student for study.   On sec-
tion, however, the organ was found to contain a large number
of cavities, and Professor Hamann gave me the specimen for
investigation.   Professor Hamann tells me that similar holes
are not very uncommonly found in the brains of dissecting-
room cadavers, and that the condition is usually attributed to
imperfect hardening.

Description of the brain.   The organ is of ordinary size.
The convolutions, sulci, meninges, and the structures at the
base are normal in appearance.   Section of both cerebral
hemispheres shows great numbers of holes, cysts, or empty
spaces varying from a pin's point to three centimetres in
diameter.   The greater number are between two and five
millimetres in diameter.   They are usually round or oval in
outline, but some are very much elongated.   A few of these
cysts are situated in the gray matter of the cortex.   They are
found in greatest numbers in the white matter throughout the
cerebrum, which in many places s simply filled with small
cavities, many of which communicate with each other.   The
internal and external capsules and the various nuclei are filled
with similar cysts.   All of these cysts are empty and have
smooth walls.   Here and there in the centre of the hemi-
spheres where the cysts are very close together the tissue is
soft and friable.   There are, however, no areas of abscess
formation, and no appearances suggestive of inflammatory
reaction are to be seen.

The cerebellum contains large numbers of cysts similar to
those described in the cerebrum.   The cysts are most nu-
merous in the central portion of the organ.   The ventricles
appear normal.

Histological examination of sections of various portions of
the brain stained with hematoxylin and eosin, methylene

blue and eosin, and with Weigert's fibrin stain, shows in
general the same appearances everywhere. Three varieties
of holes or cysts can be made out. (1) Very large round,
oval and long oval cysts, plainly visible to the naked eye,
and measuring from one to thirty millimetres in diameter;
(2) small cysts the size of a pin's point or slightly larger,
which can be seen when the section is held up to the light;
and (3) cysts of microscopical size.

On microscopical examination all of the cysts are very
much alike; they contain no lining membrane, but are simply
spaces or holes in the brain tissue, which almost everwhere
shows no discernible change except condensation from pres-
sure. The walls are in general smooth, but in some, es-
pecially some of the small ones, the outline of the cyst is
irregular and jagged, and the tissue for a short distance is
disintegrated, does not stain, and the nuclei have disappeared.
This appearance is, however, quite exceptional. Along the
walls of the cysts of all sizes and appearances there are va-
riable numbers of bacilli, which occur singly, in groups of
three or four, and in large or small clumps. The large
clumps are always elongated and stretched along the cyst
wall; they are never found in round or oval clumps of any
size. The large and the medium-sized cysts are apparently
quite independent of blood or lymph vessels, but many of
the smaller cysts, and especially those of microscopic size,
bear an intimate relation to the blood vessels. Many of
them are seated to one side of, while some quite surround,
an artery, a vein, or in some places a capillary. In these
cases it is evident that the cyst formation is due to dilatation
of the perivascular lymph spaces. In many places, long
oval spaces containing bacilli are seen at one side of arteries
and veins cut longitudinally. In some places the lumina of
the vessels are evidently dilated, and in some of them they
had ruptured and opened into the cysts.

The brain tissue in general is remarkably well preserved.
The nuclei of the ganglion cells and of the glia cells stain
well.

*Bacilli.* Bacilli are found in variable numbers in arteries,

veins, and capillaries, along the cyst walls, and here
and there are small clumps in the tissues. Most of the
blood vessels, including the small arteries, are filled with
bacilli, and are often crowded with them. The bacilli in many
places fill the lumina of the blood vessels; they are some-
times, however, collected in the centre and sometimes form
a wall about the margin of the vessels. The bacilli are every-
where alike and are in pure culture. They are stout, meas-
uring 0.5 $\mu$ in their transverse diameter. They vary con-
siderably from 1 to 6 or 8 $\mu$ in length. They usually have
rounded ends, and about many a clear halo can be made out.
No spores or capsules can be made out. Morphologically
the bacilli are identical with B. aërogenes capsulatus.

*Case VI.* — Summary. Multiple small cavities in the white
matter of the frontal and parietal lobes and internal capsules
of the cerebral hemispheres and of the cerebellum, containing
bacilli morphologically identical with B. aërogenes capsulatus.

A man aged 53 years, a patient of Dr. La Dow, died of
arterio-sclerosis April 8, 1900, at Warrensville, Ohio. The
autopsy was made forty-eight hours after death by Dr. R. G.
Perkins. The weather was cold. Anatomical diagnosis:
Arterio-sclerosis, fibroid myocarditis, chronic interstitial
nephritis, hydro-thorax. Chronic passive congestion of all
the organs. Cavities of the brain associated with the presence
of Bacillus aërogenes capsulatus.

The body was cold, fairly well preserved; rigor mortis
present. The skin was free from edema, wounds, or abra-
sions. The subcutaneous tissue showed no gaseous emphy-
sema. On section no gas was found in the abdominal or
thoracic cavities and organs or blood vessels. Aërobic cult-
ures from the various organs remained sterile.

Brain. — The superficial vessels contained no gas bubbles.
The arteries were thickened.

At the autopsy, incisions into the brain were limited to
the lateral ventricles, in which nothing unusual was found.
Complete section of the brain was reserved until after it was
hardened in formalin, when on examination a number of
smooth-walled cavities measuring from one to four or five

millimetres in diameter were found in the white matter of the frontal and parietal lobes and the internal capsules of each side, as well as in the cerebellum. These cavities were oval or round in outline. On microscopical examination they were regular in outline, without a lining membrane, their walls being composed of somewhat compressed brain tissue. There was no necrosis or disintegration, and the neighboring brain tissue stained fairly well. Seated at one side of many of the smaller cavities a medium-sized artery or vein could be made out. In some of these vessels there were large stout bacilli. Similar bacilli, occurring singly and in pairs, end to end and in clumps, were found along the walls of the cavities, and often in considerable numbers in the surrounding tissue, and in the blood vessels of all sizes. Besides the large cavities, there were some of microscopical size situated about small veins and arteries, and containing similar bacilli. There was no inflammatory reaction. Many of the cavities were evidently due to dilatation of perivascular spaces.

The large bacilli were present in pure culture and in large numbers. They stained well with hæmatoxylin, methylene blue, and Weigert's fibrin stain. Spores and capsules were not found, but about many a distinct halo could be made out. Morphologically they were identical with B. aërogenes capsulatus.

I am well aware that the proof that the bacilli of the last two cases were B. aërogenes capsulatus is not absolutely conclusive, but in the light of Reuling's and Herring's case, my own previous observations, and the facts that aërobic cultures were negative in one case (Case VI.), the morphological and staining characters of the bacilli, and the absence of knowledge of other bacilli of their size and appearance capable of forming gas in the tissues, I feel justified in believing that these bacilli are to be classed with B. aërogenes capsulatus.

Small cavities are not infrequently found in the brains of persons dying of general paralysis of the insane and other chronic diseases of the central nervous system. In many of these cases the appearance of the brain has been likened to that of " Gruyère " cheese. The cavities have been described

as being round or oval in outline, with smooth glistening walls, often traversed by a blood vessel and always without a lining membrane. They varied in size from a pin's head to a pea or bean, the smaller size being more common. They were found most commonly in the frontal and central portions of the cerebral cortex, often in the nuclei, and occasionally in the medulla and pons. Lockhart Clarke[6] (1870), H. Obersteiner, Jr.[7] (1872), Ripping[8] (1874), and Schlesinger[9] (1879), attributed them to dilatation of the perivascular lymph spaces. Berkley[10] (1900), without mentioning these cysts, lays stress upon dilatation of the perivascular lymph spaces of the brain due to cell accumulation and pressure in general paralysis of the insane.

Arndt[11] regarded them as due to shrinking of the tissues in the process of hardening. Schüle[12] calls the process a rarifying encephalitis due to the distension of the network of the neuroglia on account of lymph stasis. Weisinger[13] (1874) attributed them to dilatation of the pericellular spaces of the neuroglia. Atkins[14] (1876) recognized the possibility of small cerebral cysts having their origin in the dilatation of the perivascular lymph spaces, but thought the most important factor in their production was arterial sclerosis of the cerebral vessels, leading to circumscribed dilatation of small vessels with transudation of their contents into the neighboring tissues, compressing of the latter, filling up of the perivascular lymyh spaces, and infiltrating the adjacent brain tissue. He thought that the cyst-like cavities which were often traversed by a vessel were produced by the disintegration of these elements and called the process "cystiform degeneration." Gray[15] had previously (1874) suggested that the cavities of a brain having the "Gruyère cheese" appearance were due to absorption of the nerve cells and fibres brought about by pressure of areas of induration. None of these authors mention gas cysts or gaseous emphysema of the organs.

Savage and Hale White[16] in 1884 exhaustively discussed the causes of "holes in the brain," which, they pointed out, may be produced in a variety of ways. They refer to the cases of two general paralytics with "cystic degeneration"

of the kidneys, liver, lungs, heart muscle, and brain. The
renal cysts involved either glomeruli or tubules; the livers
had a spongy appearance, their cavities were apparently due
to vacuolar degeneration of the liver cells and were not con-
nected with the bile ducts; the lung cavities were circular,
unconnected with bronchi, and often occurred in groups; the
cysts of the heart muscle were similar to those of the other
organs. Some of these cysts contained a peculiar amorphous
material which stained brightly with logwood; none of them
showed a lining membrane. The brains contained a number
of cleanly punched out cavities without lining membranes and
closely resembling the " Gruyère cheese " brain, for which
they state many pathologists would take the brains of these
two cases. Savage and White do not commit themselves to
any particular explanation of the origin of the brain cysts in
their cases, but exclude as possible causes contraction of the
neuroglia and dilatation of the lymph spaces; the latter, as
we have seen, being the most common interpretation of the
cysts in the "Gruyère cheese" brain. They suggest the
possibility that the brain cysts of their cases were due to
degeneration of the nervous elements and describe the whole
process in all the organs under the title of " universal cystic
degeneration." They fail to give a detailed report of the
autopsy findings. No mention is made of the presence of
gas in any of the organs. In a second paper Savage and
White [17] emphasize the point that the cysts of the livers of the
cases reported in their previous paper were due to vacuolar
change in the liver cells and not to post mortem change or
to dilatation of the bile ducts. They state that there were
no bacilli in sections of these livers, and that livers containing
gas cysts of bacterial origin fail to show the peculiar vacuolar
changes found in these cases. They argue, therefore, that
the cysts of the brain, liver, and other organs of their two
cases differed entirely in their origin from those seen in post-
mortem decomposition of organs. They also describe a
specimen of the " Gruyère cheese " brain, the cavities of
which they think are due to the dilatation of the perivascular
lymph spaces. In their first article Savage and White

classify the various conditions causing holes in the brain as follows:

(1) Depressions on the surface of the brain resulting from the pulling out of small processes of adherent membrane in general paralysis. (2) Contraction of sclerosed neuroglia. (3) Multiple hydatids. (4) État criblé of Griesinger, due to extreme congestion of the cerebral vessels- (5) Shrinking of the cerebral convolutions. (6) Pressure of miliary aneurysms upon the brain substance. (7) Porencephalic cavities. (8) Gruyère cheese brain. (9) General cystic degeneration affecting the brain with other viscera.

There can be no doubt that cysts of the brain may have their origin in many of these ways, besides in the degeneration and necrosis of tumors and areas of hemorrhage, and by gas-forming micro-organisms.

It is very difficult to classify according to their origin the various brain cavities described in the literature. Most of them occurred in the brains of individuals with general paralysis of the insane, chronic insanity, idiocy, and epilepsy, in many cases of which there was ample opportunity for pressure upon perivascular lymph spaces by cellular exudations, and vascular dilatations, and degenerations and sclerosis, minute hemorrhages, etc. In the case reported by H. Obersteiner, Jr.,[7] there was a gumma of the medulla about which there were a number of cavities the size of a pin's head. He attributed the cyst formation to dilatation of the perivascular lymph spaces, some of which were plugged with round cells. It is difficult to determine the part played by degeneration of the brain tissue in the production of these cavities. It is to be noted that none of the observers, until the writer, mention the presence of gas in the brain or its vessels, or gaseous emphysema of other organs.

It is a striking fact that the illustrations of any of these cysts apply perfectly for the gas cysts of our cases. It is impossible to decide whether the cysts of any of these cases, even those reported by Savage and White, are gaseous in origin. On account, however, of the great similarity in their gross appearances and distribution (especially of those of

the so-called " Gruyère cheese " brain), and in view of their
relation to the blood-vessels, and of the microscopical appear-
ance to our cases, the brain cysts of many of these cases were
probably due to bacteria.

Many if not most of the cysts in some sections from our
cases are situated about small blood vessels. In some places
a blood vessel traverses the centre of the cavity, while in
others it is pushed to one side, and in both instances the cysts
are perivascular. Here and there in the sections of Case V.
there are dilatations of pericellular spaces, with shrinkage of
the ganglion cells. In these spaces, however, no bacilli are
found. The main difference between the brain cysts of the
older writers and those described by Reuling and Herring
and the writer, is that the former almost invariably occurred
in brains the seat of the changes of general paralysis of the
insane or other chronic nervous diseases, while the latter were
free from chronic lesions, and showed no changes but the
cysts (except acute meningitis and brain abscess in Case III.
of my series), and the presence of numbers of bacilli in the
blood vessels and about the walls of many of the cysts.

There can be no question that the gas in the cerebral
vessels and disorganized brain of Case II. were due to the
bacilli found.

### Summary.

(1.) Of the five recorded cases of brain cysts proved to
be caused by bacteria, four were due to B. aërogenes cap-
sulatus, and one to B. mucosus capsulatus.

(2.) In the two cases of gas in the blood vessels of the
brain (and in the disorganized brain tissue of one of them),
in association with general gaseous emphysema reported in
this article, B. aërogenes capsulatus was present in pure
culture in one, and with B. mucosus capsulatus in the other.

(3.) While it is impossible to determine what proportion of
brain cysts unassociated with hemorrhages, atrophy or non-
development of brain tissue and the disintegration of tumors,
described by previous writers, were due to gas-producing
micro-organisms, the seat, descriptions, and illustrations of the

cysts in many of these cases correspond in a remarkable manner to those of the gas cysts of the brain described by Reuling and Herring and myself.

(4.) More frequent and more careful examination of the brain at autopsy, especially in cases of general gaseous emphysema, will probably show that gas cysts of this organ are more common than is generally supposed.

## REFERENCES.

1. Harris. Welch. Morbid Conditions caused by B. Aërogenes Capsulatus. Bulletin of the Johns Hopkins Hospital, September, 1900.
2. Perkins. Journal of Experimental Medicine, Vol. V., p. 389.
3. Bulletin of the Johns Hopkins Hospital, 1899, Vol. X., No. 97, pp. 62–69.
4. Contributions to the Science of Medicine. Dedicated to William H. Welch, Baltimore, 1900.
5. Journal of Experimental Medicine, 1900, Vol. V.
6. J. Lockhart Clarke. Journal of Mental Science, 1870, p. 499.
7. H. Obersteiner, Jr. Virchow's Archiv., 1872, Bd. 55, S. 318.
8. Ripping. Allg. Zeitschrift f. Phsychiatrie, Bd. XXX., 1874.
9. Schlesinger. Archiv. f. Psychiatrie und Nervenkrankheiten, 1879–80. Bd. X., p. 516.
10. Berkley, H. J. A Treatise on Mental Diseases, 1900.
11. Arndt. Virchow's Archiv., Bd. LXXIII., S. 196.
12. Schüle. Quoted by Schlesinger.
13. Weisinger. Archiv. f. Psychiatrie und Nervenkrankheiten, Bd. V., 1874–5, S. 379.
14. Atkins. The Medical Examiner, London, Vol. I., 1876, p. 85.
15. Gray. American Journal of Insanity, July, 1874.
16. Savage and White. Trans. London Pathological Society, 1883, Vol. XXXIV.
17. Savage and White. *Ibid.*, 1884, Vol. XXXV., p. 214.

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## REPORT OF NINE CASES OF INFECTION WITH BACILLUS PYOCYANEUS.

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The presence of a blue or green color in the pus of various suppurative lesions was noted long before the isolation of the organism which produced this pigment, and since its discovery there have been many reports of its presence in a variety of pathological conditions. None the less, its occurrence is not so frequent as to be unworthy of notice, especially when the infection atrium, the lesion, or the distribution is an unusual one for this organism.

In the following summary of the literature on B. pyocyaneus up to the present time such references as are not otherwise noted can be found in the articles of Lartigau, Blumer, and Barker.[1]

The relation of B. pyocyaneus to the blue or green coloring matter found at times in suppurating wounds was first established by Gessard, and the organism was for some time considered merely as a saprophyte. It has been described as such, — unrelated to any pathological lesions, — in the saliva by Pansini, in the sputum by Frisch, in cultures from the nose and throat by Gorham,[2] in the stomach by Abelous, and in the sweat by Eberth and Audovard. Its frequency in suppurating wounds in comparison with other organisms is but small, as shown by Jakowski, who found it only twice in 200 cases.

Its definite relation to pathological processes was first well established by Charrin, though Ledderhose had previously made experiments on animals. B. pyocyaneus has been found in skin lesions, usually of an ecthymatous type, by Barker, Ehlers, Hitschman and Kreibisch,[3] Karlinski, Oet-

tinger, Jadkewitsch, and Triboulet; in furuncles of the external auditory meatus by Maggiora; in acute otitis media by Babes,[13] Gruber,[4] Harbitz,[5] Kossel, Maggiora and Gradenigo, Martha, Pes and Gradenigo, and in chronic otitis media in nine cases by Kanthack;[6] also in panophthalmia by Sattler.[7] Its presence in lesions of the respiratory tract has been reported in ozæna, with other organisms, by Walter Stein;[8] in acute angina simulating diphtheria by Blumer; in bronchiectasis by Barker; in broncho-pneumonia by Barker and Monnier; in gangrene of the lung, in association with cocci, by Hirschler and Terray;[9] and in tuberculous cavities by Koch. In the digestive tract it has been described in noma by Monnier; in carious teeth by Arkovy;[10] in œsophageal lesions by Barker; in ulcerative gastritis by Wollstein;[11] in cholera nostras by Pottien;[12] in diarrhœas of infants by Booker, Neumann, Williams, Thiercelin and Lesage; in dysentery by Barker, Bertrand and Baucher, Calmette, Lartigau, and Maggiora; in appendicitis, associated with staphylococcus aureus, by Kelly.[13] Pyocyaneus infections of the serous membranes have been found by Lartigau in the pleura, and Barker and Ernst in the pericardium, Barker and Lartigau in the peritoneum. In lesions of the synovial membranes it has been found in prepatellar bursitis by Schürmayer,[14] and in joints, associated with the tubercle bacillus, by Pawlowsky.[15] Barker and Blum[16] have described cases of acute endocarditis, with general distribution throughout the body. In the urinary tract the organism has been found in cystitis, both acute and chronic, by Barker, Bernhardt,[17] Brown,[18] Jadkewitsch, Le Noir, McWeeny,[19] Motz, and in infections of the ureters and kidneys by Barker, in association with B. proteus vulgaris by Blumer and Lartigau. It was found in two cases of liver abscess by Kruse and Pasquale, and in chronic mastitis by Charrin. In the female genital tract Barker found it in a case of ovarian abscess, Laplace[20] in six cases of endocervicitis associated with the pyogenic cocci, and Charrin in one case of puerperal sepsis. Four cases of pyocyaneus meningitis are reported by Honl, Kossel, Pesina, and Councilman,[21] the

last case in association with staphylococci. Primary infection of the umbilical cord with this organism was found in one case by Babes. Two cases are reported by Karlinski, in which the bacillus was found in cases of pyemia, each time in association with staphylococcus aureus. Jadkewitsch reports one case of the nervous type of infection with pyocyaneus.

Cases of general infection, usually secondary to some primary lesion, in which B. pyocyaneus was found in wide distribution are reported by Barker, Blum, Calmette, Ehlers, Finkelstein, Karlinski, Krannhals, Lartigau, Monnier, Neumann, Oettinger, Williams and Cameron, and Wollstein.

In the last three years the writer has met with B. pyocyaneus in nine cases. Six of these occurred in the routine examinations of cultures from 217 autopsies at Lakeside Hospital, and 3 in patients outside the hospital. In 800 autopsies at the Johns Hopkins Hospital the organism was cultivated only 11 times, making the average frequency in 1,017 autopsies about one in 60, or 1.66 per cent. Cases I. and II. show a portal of entry described only once, by Charrin, the uterine mucosa in puerperal septicæmia, together with the presence of the bacillus in internal and presumably secondary purulent lesions, one of which has been recorded four times, and one twice.

*Case I.* — Puerperal septicæmia with fibrino-purulent endometritis and purulent cerebro-spinal meningitis and ependymitis with the presence of B. pyocyaneus in pure culture in the cerebro-spinal exudates and in the liver, and in the uterus in association with staphylococci.

This case gains additional interest from the presence of a well-marked glycosuria, apparently central in origin, due perhaps to irritation of the diabetic centre in the floor of the IV. ventricle. The areas of Langerhans in the pancreas showed none of the lesions described by Opie[21] in cases of pancreatic diabetes, nor were any other lesions of the pancreas noted in microscopical examination.

*Clinical Brief.* — G. C. Female, 25 years old. Entered the Lakeside Hospital Dec. 23, 1900, complaining of severe pains

in the limbs, back, and head, especially in the cervical spine and in the occiput. There was no family history of tuberculosis. The patient had had whooping cough, diphtheria, influenza, and typhoid fever, but none of these recently. Six weeks previous to admission she had had a miscarriage, and there had been discharge from the vagina ever since, though she was not conscious of any fever.

Physical examination of the chest and abdomen revealed nothing of importance. Vaginal examination showed a soft, somewhat enlarged uterus, with a foul-smelling discharge from the cervix. The urine contained a trace of albumen, with a few casts, and gave a well-marked sugar test with Fehling's solution. The presence of sugar persisted till death. The blood on admission showed 72 per cent. of hæmoglobin, and a leucocytosis of 14,000, which increased to 32,000 the day before death. The temperature on admission was 100.5° C. and varied from 96° to 103.2°, the last taken being 103°. The pulse on admission was 90, but it rose steadily, reaching 180 the day before death. The patient complained of much pain, and had marked opisthotonos and inequality of the pupils. She became rapidly worse, sank into a comatose condition, and died eight days after admission. Her condition was never such as to admit of any operation. Clinical diagnosis: meningitis, probably tubercular. The autopsy was held 19 hours after death, the body having been in cold storage at 0° C.

*Pathological Brief.* — Anatomical diagnosis. Fibrino-purulent endometritis after abortion. Fibrino-purulent cerebro-spinal meningitis and ependymitis, with the presence of B. pyocyaneus in the uterine and cerebro-spinal exudates. Congestion, œdema, emphysema, and atalectasis of the lungs. Cloudy swelling of the liver and kidneys. Corpus luteum of pregnancy in the left ovary. General chronic passive congestion.

The abdominal and thoracic organs showed nothing of present interest. There was no peritonitis. The left ovary showed a corpus luteum of pregnancy. The tubes were apparently normal. The uterus was rather large, soft, and

filled with an exceedingly foul-smelling brownish semi-fluid material. At the upper right-hand side of the uterine cavity just below the cornu there was an adherent mass 1 × 1 × .5 cm. in size, soft and necrotic, suggesting placental remains. Examination of the head showed no abnormality in scalp or skull. The vertex and the ventral portions of the brain were negative, the base was covered with a thick yellowish-white purulent exudate, rather firm in consistency, filling up all the crevices of the lower surface.

It extended from the ventral border of the pons, dorsally to the medulla and cord, and down the cord to its extreme lower end. Examination of the ventricles showed purulent fluid with a heavy sediment of pus, but no adherent exudate, the process being apparently of later date than that on the surface of the brain. All the ventricles were involved. The sinuses showed no thrombi or other changes. None of the exudates, either uterine or cerebral, showed any blue or green color.

Cultures were taken as is usual in our autopsy routine from all the organs and all the pathological exudates. Coverslips were made from the uterus, the meninges, and the ventricles. Coverslips from the uterus showed a large variety of organisms including cocci and numerous slender bacilli, staining irregularly with methylene blue; a few large stout bacilli were also present. Coverslips from the meningeal exudate and from the ventricles showed numerous long, rather slender bacilli which showed a marked tendency to irregular staining, after the manner of the Klebs-Loeffler bacillus, to which they bore a close resemblance.

Cultures from the heart, spleen, and kidneys, kept at 37° C. for 48 hours, showed no growth. Cultures from the lung showed fairly numerous colonies of a large, unidentified coccus, not pathogenic for rabbits. Cultures from the base of the brain, from the ventricles, and from the spinal cord showed very numerous colonies, those on the surface large, spreading, blue in color, many with a rather concentric appearance. Homogeneous under the low power. The colonies in the depth were opaque and yellowish. The plates

had a strong, sickly, sweet odor, resembling that of the pyocyaneus group.

Cultures from the liver showed a few colonies of the same type.

Cultures from the uterus showed a variety of colonies, most numerous of which were colonies like those in the brain and liver plates, associated with colonies of the yellow and white staphylococci. The plate had an odor similar to the plates from the brain and cord.

Coverslips from these colonies showed rather long bacilli, staining irregularly with Loeffler's methylene blue, many of them with slightly clubbed ends. Examination by the hanging-drop method showed no motility.

Transplantations were made into various media, with the result that the growths and characteristics changed materially, until the third and fourth generations, since when no change has been noted.

The first generation showed no color, no motility, and very slight liquefactive powers, but with successive transplantations the color became a dark green, the motility became marked, and the power of liquefaction increased, until now the cultures answer well to the usual descriptions of B. pyocyaneus.

Throughout the cerebro-spinal tract and in the uterus, two varieties were isolated, both forming green pigment, and only differing from one another in the vigor of their growth, and in their chemical activities. The liver colonies all belonged to one variety.

The essential cultural characteristics of both organisms were as follows, in 24-hour cultures:

Glycerin agar. Grayish-green, moist, translucent growth with wavy edges; water of condensation cloudy, greenish, medium uniformly light green. Growth to bottom of stab, no gas.

Glucose. Same. No gas.

Bouillon. Light green color with well marked fluorescence, distinct viscidity, grayish scum on surface, medium cloudy throughout; no sediment.

Litmus milk. Reaction unchanged.

Human blood serum. Medium greenish. The growth lies in a trench made by beginning liquefaction.

Gelatin. No liquefaction.

Potato. Light brown growth; water of condensation cloudy, potato not discolored; sickly, sweet odor well marked.

In cultures two to twelve days old, both milk and blood serum were peptonized without change of reaction, the filtered solution giving the Biuret test for peptone; gelatin tubes were liquefied completely in 10 to 12 days, the lique-faction early reaching the sides of the tube, the growth on potato became more markedly green, and the odor on all media was more distinct.

Coverslips from the cultures, after the second generation, showed short rather oval bacilli 1.0 to 1.5 $\mu$ in length, by 0.33 to 0.50 $\mu$ in width, which were actively motile and decolorized by Gram's method. Owing to the depth of the color, and to the change of the blue to red when acidulated, the indol test was difficult of demonstration, but it was thought that a posi-tive reaction was obtained in the earlier generations, though not later, agreeing with Jordan's observations.[23] Extraction with $CHCl_3$ revealed the presence of pyocyanin in large amount.

*Microscopical Descriptions.* — The liver and spleen showed well-marked congestion and cloudy swelling. The pancreas showed no changes, either in the areas of Langerhans, or elsewhere. The other abdominal and thoracic organs showed nothing of present interest. The uterus was markedly con-gested, the mucosa was lost in places, and covered with a thick, fibrinous exudate, containing numerous polymorpho-nuclear leucocytes and plasma cells. Large numbers of short, slender bacilli were seen together with a smaller number of cocci and some few large, stout bacilli with rounded ends. The infiltration with cells, and the presence of the slender bacilli, extended to a considerable depth below the mucosa.

Sections through the meninges and through the under-lying tissues of the brain and cord showed a thick fibrino-

purulent exudate, apparently firmly adherent to the tissue beneath. The exudate next to the nervous tissue was composed of large numbers of plasma cells, with some small round cells, and occasional eosinophiles and mast cells. Further out the exudate was more acute in character and was composed chiefly of polymorphonuclear leucocytes. Fibrin was present only in small amount. Staining with Weigert's fibrin stain showed no bacteria, but eosin and methylene blue brought out a small number of slender bacilli, with a rather irregular stain. The brain and cord beneath the exudate showed a well-marked chronic inflammatory reaction, the vessels were surrounded with an infiltration of small round cells, and no polymorphonuclear leucocytes or bacteria were noted in the tissues. Sections through the walls of the lateral ventricle showed a purulent exudate without fibrin, and a well-marked infiltration of the tissue in the neighborhood, with fibrinous thrombi in the small veins. A moderate number of bacteria was found both in the exudate and in the brain substance, closely resembling the organisms seen in the meningeal exudate.

*Animal Experiments.* — Inoculations of guinea pigs gave no result. A rabbit inoculated at the root of the ear with ½ c.c. of a 24-hour bouillon culture died in two weeks with extensive subcutaneous abscess formation, from which B. pyocyaneus was recovered.

*Case II.* — Puerperal septicæmia, with purulent endometritis, broncho-pneumonia with abscess formation in the consolidated areas. B. pyocyaneus was found in pure culture in the uterus, and associated with a small number of large, unidentified bacilli in the lungs.

*Clinical Brief.* — Negress, 21 years of age. Died Sept. 28, 1899, in the service of Dr. Hoover at the City Hospital of Cleveland, a few days after admission. The only history obtainable was that of a full term delivery six weeks previous to admission, and the onset of chills and fever a few days after the birth of the child.

*Clinical Diagnosis.* — Puerperal infection. Thrombosis of pulmonary arteries, broncho-pneumonia and multiple ab-

scesses of both lungs. Acute splenic tumor. Cloudy swelling and fatty degeneration of the liver and kidneys, with acute parenchymatous nephritis.

*Lungs.* — There was marked oedema with multiple areas of recent broncho-pneumonia, varying considerably in size. Some of these, from 2-3 cm. in diameter, showed central softening with the formation of small cavities containing foul-smelling, grayish-yellow pus. This condition involved the entire right lung, but only the lower lobe of the left lung. Both pulmonary arteries showed recent, non-adherent, grayish-red thrombi in their branches.

*Uterus.* — Somewhat enlarged, endometrium dark red in color, but without fibrinous exudation. The other organs showed nothing of present interest. No gas was found in any organ.

Coverslips from the lungs in the consolidated areas, and from the uterus showed numerous small, rather slender bacilli, and some large, stout bacilli. Aerobic cultures were made from the various organs, but all remained sterile save those from the uterus and lungs. Cultures from both of these showed a slender bacillus which stained by Gram's method and was actively motile. It peptonized milk without formation of acid, and was otherwise similar to the organism found in Case I.

*Microscopical Description.* — Uterus. The mucosa was lost for the most part. The underlying tissues were deeply infiltrated with polymorphonuclear leucocytes, and with a large number of small, rather oval bacilli. On the surface of the mucosa these bacilli were associated with a few large, stout bacilli with rounded ends.

Sections from the consolidated areas of the lungs showed well-marked broncho-pneumonia. The alveoli were filled with an exudate composed of polymorphonuclear leucocytes, with here and there a small amount of fibrin. In numerous areas the alveolar walls were broken down, with formation of small abscesses, filled with polymorphonuclear leucocytes, many of which showed marked nuclear fragmentation. Sections stained with eosin and methylene blue showed very

large numbers of bacteria, of which a few were large and
stout with rounded ends, but most of which were slender,
some much longer than others, many showing a slight curve.
They stained irregularly with methylene blue, and sharply
by Gram's method. They occurred in greatest numbers in
and about the abscesses, though present everywhere in the
consolidated areas.

*Case III.* — Scirrhus carcinoma of the pylorus, gastroen-
terostomy, with subsequent fœcal fibrino-purulent peritonitis.
B. pyocyaneus was present in pure culture in the peritoneal
exudate.

*Clinical Brief.* — H. S. Male, 30 yrs. old. Admitted to
Lakeside Hospital for gastro-enterostomy operation for car-
cinoma of pylorus. Post-operative peritonitis developed,
with death as a result.

*Anatomical Diagnosis.* — Scirrhus carcinoma of stomach
with metastases in liver and in mesenteric lymph glands,
fibrino-purulent peritonitis, sero-fibrinous pleurisy, and peri-
carditis. Chronic adhesive apical pleurisy with chronic
fibroid apical tuberculosis and apical tubercular pneumonia;
congestion and emphysema of lungs with unresolved pneu-
monia; congestion of liver, spleen, and kidneys; fatty liver,
interstitial splenitis, cloudy swelling of kidneys. Healed
gastro-enterostomy and recent gastro-enterostomy, with gas-
tro-peritoneal fistula.

The organs showed the changes noted in the anatomical
diagnosis. The peritoneum contained 1,500 c.c. of yellow
fluid, containing many fibrin flakes, and having a markedly
fecal odor.

Coverslips and cultures from the pneumonic areas in the
lungs and from the pleura and pericardium, showed diplo-
coccus lanceolatus in pure culture. Coverslips from the
peritoneal cavity showed large, stout capsulated bacilli and
small, slender bacilli, staining irregularly with methylene
blue. Cultures showed a short, slender bacillus, actively
motile, which decolorized by Gram. It peptonized milk
with acid reaction and coagulation, and bore a close resem-
blance to the organisms previously described.

*Case IV.* — Acute orchitis in typhoid (?) fever with the presence of B. pyocyaneus in pure culture·in the testicle.

*Clinical Brief.* — Male, white, 27 years old. Admitted to the City Hospital with a mild case of supposed typhoid fever. A few days after admission, one testicle became large and tender, and the patient was transferred to the service of Dr. C. A. Hamann, who did an orchidectomy. There was no actual purulent exudate, but the tissue was markedly softened.

*Pathological Brief.* — Cultures were made and studied at the Pathological Laboratory of Western Reserve University, and showed a pure growth of an actively motile, slender bacillus which decolorized by Gram's method. Litmus milk was rapidly peptonized without change in reaction, and the general cultural characteristics closely resembled those of the organisms described in the previous cases. Microscopical sections of the testicle and epididymis showed well-marked purulent infiltration, with the presence of large numbers of eosinophiles and a few mast-cells.

*Case V.* — Pustular eruption of an ecthymatous type on the inner surfaces of the thighs, with the presence of B. pyocyaneus in pure culture.

Negro, 40 years old. Admitted to the City Hospital in 1898, with enlarged glands in the neck, groins, and axillæ, and a pustular ecthymatous eruption on the inner surfaces of the thighs. A clinical diagnosis of glanders was made and cultures were taken from the pustular lesions. These cultures were studied at the Pathological Laboratory of Western Reserve University; they showed a pure culture of a short bacillus, rather slender, and often occurring in thread-like forms, — by Gram's method, and actively motile. The growths on the various media closely resembled those of the organisms in the previous cases. Diagnosis B. pyocyaneus.

*Case VI.* — Abscesses about seventh rib of the left side and in the left elbow joint, with the presence of B. pyocyaneus in pure culture in both abscesses.

*Clinical Brief.* — Male, 30 years. Admitted to the medical wards of Lakeside Hospital, Oct. 10, 1899. He had just

had pneumonia, and physical examination showed the presence of fluid in his chest. Shortly after admission a fluctuating area was noted in the left axilla about the seventh rib, and he soon developed an acute arthritis of the left elbow joint. He was transferred to the surgical service for operation, and both abscesses were opened. They contained large quantities of greenish, foul-smelling pus, and no connection between the abscess about the rib, and the pleural cavity could be found. The patient's temperature continued at about 102°, with a pulse of 112, and upward, and he died a few days later. Autopsy was refused.

*Pathological Brief.* — Coverslips from both abscesses showed short, slender bacilli. Cultures showed a short, slender bacillus, motile, decolorizing by Gram's method and closely resembling the organisms described in the previous cases. Resection of a rib in the floor of the abscess showed that there was no empyema, but a sub-acute fibrinous pleurisy. The mode of examination forced upon us made cultures from the pleural cavity impossible.

*Case VII.* — Acute diarrhœa. Broncho-pneumonia. General congestion of organs. Presence of B. pyocyaneus in small numbers in all the organs.

*Clinical Brief.* — Male, black, 4 months old. The patient had had diarrhœa for a week, with numerous green dejections. He also had frequent spasms, almost amounting to convulsions, since the onset of the disease. The abdomen was tender and the peristalsis was violent. The child became rapidly emaciated and died of asthenia.

*Pathological Brief.* — Anatomical Diagnosis. Congestion, atalectasis, broncho-pneumonia of lungs; congestion and fatty degeneration of liver; congestion of spleen and kidneys and of gastro-intestinal tract.

Cultures from the various organs showed small numbers of colonies of a bacillus which was motile, decolorized by Gram's method, and otherwise resembled the bacilli found in previous cases. Unfortunately no cultures were made from the intestines.

The organs showed cloudy swelling and congestion, and

the mucosa of the stomach and intestines showed well marked congestion, but no ulcerations.

Besides these seven cases, B. pyocyaneus was found twice where its association with existent pathological lesions is rather suggested than definitely proven.

*Case VIII.* — Œdema and congestion of the lungs, with the presence of B. pyocyaneus in large numbers in pure culture. Congestion and cloudy swelling of the liver and kidneys; lymphoid hyperplasia in the gastro-intestinal tract. Miliary abscesses of the brain, with the presence of a bacillus similar in morphology and staining reactions to that found in the lung, but not cultivated.

*Clinical Brief.* — Boy two months old. Admitted to the children's ward of Lakeside Hospital. He had had diarrhœa for the last three weeks with marked progressive emaciation, and died under the clinical diagnosis of malnutrition.

*Pathological Brief.* — Anatomical diagnosis: Miliary abscesses of the brain. Congestion, fatty degeneration, and cloudy swelling of the liver and kidneys; emphysema, œdema, and congestion of the lungs.

Cultures from all the organs except the lung were negative. Cultures from the lung showed numerous colonies of short, slender bacilli, actively motile, and decolorizing by Gram's method. The growth on culture media and the chemical characteristics were similar to those of the organisms in the previously described cases.

Sections from the brain about the abscess cavities showed necrosis of tissue with very slight leucocytic infiltration. At the edge of the necrotic area, and throughout the vessels on the section, were large numbers of bacteria. These were of two sizes, one small, slender, and staining irregularly, the other large and stout, resembling B. aërogenes capsulatus. Both these bacilli stained well with methylene blue, but sections stained by Weigert's method show no bacteria whatever, thus excluding B. aërogenes capsulatus, which stains by Gram's method.

The fact that the organisms decolorize by Gram, together with consideration of their morphology, suggests their identity

either with B. mucosus or B. pyocyaneus brain abscess. It is
not improbable that the organisms in the brain and in the
lung are one and the same.

*Case IX.* — Burns of the third degree, with congestion and
cloudy swelling of the organs, and the presence of B. pyocy-
aneus in the heart's blood.

*Clinical Brief.* — F. F.   Male, five years.   Entered the
Lakeside Hospital Aug. 1, 1899, with extensive burns of the
third degree, and died the next day.

*Pathological Brief.* — Anatomical diagnosis : Infected burns
of third degree involving about two-thirds of the skin surface.
General congestion of organs.   Cloudy swelling of liver and
kidneys.   Chronic interstitial splenitis and hyperplasia of
mesenteric lymph glands.

The organs showed nothing but cloudy swelling.

Coverslips from the pus on the surface of the body showed
cocci, singly and in chains, and numerous short, slender
bacilli.   Cultures from the organs were negative, with the
exception of the plate from the heart's blood, which showed
a few colonies of small, slender bacilli.   Cultivation of these
showed a bacillus which was actively motile and decolorized
by Gram's method.

The cultural characteristics closely resembled those of the
organisms in the eight previous cases.

The organisms from these nine cases were carefully studied,
as well in their morphological and cultural characteristics as
in their relations to one another and to stock cultures of B.
pyocyaneus obtained from the Johns Hopkins Hospital.   The
variations from this culture and from each other were of
degree rather than kind, but some general points seem
worthy of note.

The irregular staining with methylene blue, noted by
Jordan,[20] was observed in every case, both in sections from
hardened tissues, and in coverslips from exudates or artificial
media, and in one case, in which the organisms were of un-
usual length, was so marked as to bear a close resemblance
to the Klebs-Loeffler bacillus.

In the reactions of the various organisms to Gram's stain,

my results did not coincide with those of Jordan [24] and Ru-
zicka,[25] who note complete decolorization in every case. Of
the ten varieties studied in this present series, seven decolor-
ized uniformly and regularly when treated by this method,
but three retained their color at every trial. Of these three
only one was associated with tissue lesions studied micro-
scopically; in this case (Case II.), as noted above, Weigert's
fibrin stain showed the bacilli in undiminished numbers in the
tissues, while in those cases in which the organisms decolor-
ized by Gram's method, no bacteria could be found in sections
treated according to Weigert.

The cultures on agar and on potato varied in their color
production and in the profusion of their growth, but in every
case the green color, the staining of the potato, and the odor
were characteristic of B. pyocyaneus. Ernst's chameleon
phenomenon was not seen in any of the cases.

All the varieties liquefied blood serum and peptonized lit-
mus milk, though only three cases (III., V., and VI.) caused
acid reaction on coagulation of the casein, the media in the
other seven cases remaining blue or violet and fluid until the
process was complete and the litmus discharged. The fil-
trates from milk and serum cultures, kept ten days or more
at $37^\circ$ C., gave a sharp, positive reaction to the Biuret test for
peptone.

The pigment formation was studied in six of the cases with
the result that all of them fell within variety $a$ of Jordan's
classification; namely, that variety which produces both
pyocyanin and a fluorescent pigment. Cultures from the
other four cases were less carefully studied, but one of them
(Case VII.) was so much lighter in color than the rest, even
on old cultures on agar, that it is probable it would have been
found to coincide with variety $\gamma$, fluorescigenic only.

### Summary.

In nine cases of pyocyaneus infection observed in the last
three years, two found their portal of entry in the uterine
mucosa, in puerperal septic endometritis, and gave rise sec-
ondarily, in Case I. to cerebro-spinal meningitis and epen-

dymitis, and in Case II. to broncho-pneumonia with abscess formation. Case III. adds a third to the previously reported cases of peritonitis, and was secondary to a ruptured gastro-enterostomy for carcinoma of the pylorus. Case IV. records a lesion hitherto undescribed in connection with B. pyocy-aneus, an acute orchitis in late typhoid (?) fever. Case V. adds one to the cases already on record of B. pyocyaneus in pustular skin lesions. Case VI. brings out the third recorded case of infection of the synovial membranes, the organism having been found in the elbow joint, as well as in a peri-costal abscess. Case VII. shows the fourth instance of broncho-pneumonia, as well as an additional case of general bacteriæmia in children. In Case VIII. the organism was present in the lungs, with œdema and congestion, and organ-isms resembling closely in morphology and staining reactions those cultivated were found in association with miliary ab-scesses of the brain. Case IX. is one of wide-spread super-ficial burns, with infection of the burned areas, and the presence of the organism in pure culture in the heart's blood.

## REFERENCES.

1. Phila. Med. Journ., Sept. 17, 1898.
   Journ. Exp. Med., 1898, Vol. III., No. 6.
   N.Y. Med. Journ., Sept. 22, 1900.
   Journ. Am. Med. Ass., July 31, 1897.
2. Journ. Boston Soc. Med. Sci., Vol. V., p. 385.
3. Arch. f. Derm. u. Syph., Vol. L., p. 71.  (Ref. Centr. f. Allg. Path. u. path. Anat.) 1890.
4. Monatschr. f. Ohrenheilk., No. 7, p. 887.
5. Centr. f. Allg. path. Anat., Vol. X., p. 651.
6. Zeitschr. f. Ohrenheilk., 1891, p. 44.
7. Centr. f. Allg. Path. u. path. Anat., Vol. XIV., p. 26.
8. Centr. f. Allg. Path. u. path. Anat., Vol. XXVIII., p. 729.
9. Orvosi Hetilap., 1889, No. 50.  (Ref. Centr. f. Allg. Path. u. path. Anat., 1890.)
10. Centr. f. Allg. Path. u. path. Anat., Vol. XXIII., p. 967.
11. Arch. of Pediatrics, Vol. XIV., p. 11.
12. Zeitsch. f. Hygiene, Vol. XXII., p. 140.
13. Phila. Med. Journ., Vol. IV., p. 928.
14. Zeitsch. f. Hyg., Vol. XXI., p. 281.
15. Ann. de l'Inst. Pasteur, Vol. X., p. 526.
16. Centr. f. Allg. Path. u. path. Anat., Vol. XXV., p. 116.
17. Arch. f. Derm. u. Syph., Vol. LII., p. 349.
18. Johns Hopkins Hosp. Bull., January, 1901.
19. Brit. Med. Journ., September, 1894.
20. Am. Journ. Med. Sci., October, 1898.
21. Am. Journ. Med. Sci., 1898, p. 252.
22. Journ. Exp. Med., 1900–1901.
23. Jour. of Exp. Med., 1899.
24. Op. cit.
25. Cited by Jordan.  Op. cit.

# THE PATHOLOGY OF LABIAL AND NASAL HERPES AND OF HERPES OF THE BODY OCCURRING IN ACUTE CROUPOUS PNEUMONIA, AND THEIR RELATION TO THE SO-CALLED HERPES ZOSTER.[1]

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OUR knowledge of herpes zoster was very much extended by the recent contribution of Head and Carpenter.[2] These authors showed, among other things: 1. That herpes zoster (in 18 cases, at least) is associated with destructive, and usually inflammatory, changes in the sensory ganglia (posterior root or Gasserian) corresponding to the nerve supply of the part affected with herpes. 2. That in recent cases (before the eleventh day) degenerative changes are not demonstrable in either the peripheral nerves, the posterior root fibres, or the central nervous system. 3. That in cases examined after the lapse of this period degenerative changes are present in these structures and apparently correspond to the affected areas in the ganglia. Their work was based upon the study of 21 cases in all stages of the eruption. They state that before their own work there were only two well-reported autopsies on cases of herpes ophthalmicus (Wys and Sattler) and five satisfactory reports on zoster of the trunk (Lesser, Chandelux and Dubler). Von Bärensprung's oft-quoted case is classified as unsatisfactory, because, though he noted the occurrence of hemorrhage into a ganglion, he failed to mention to which of the three ganglia removed he alluded.

While this valuable communication has placed our knowledge of herpes zoster on a substantial basis, it is clear that more light is needed upon the etiological factors concerned, as well as upon the identification and classification of the various types of herpes.

[1] Read at the Seventeenth Annual Meeting of the Association of American Physicians, held in Washington, D. C., 1902.
[2] Brain, Autumn, 1900.

In order to clearly understand our present knowledge on the subject, the following summary of the main facts may be helpful.   There are a number of clinical and apparently several anatomical types of herpes : herpes zoster involving the neck, trunk, and extremities (following the distribution of the spinal posterior root ganglia); herpes ophthalmicus (following the distribution of the first division of the fifth or trigeminal nerve, Gasserian ganglion); herpes facialis, herpes labialis et nasalis (probably following the distribution of the second and third divisions of the trigeminal nerve, but unsupported at this time by anatomical observations), and herpes genitalis (commonly believed to be due to local irritation and not known to be associated with any lesion of the nervous system).

The herpes facialis, labialis, nasalis, and genitalis are classed by Hartzell[1] as herpes simplex, in contradistinction to herpes zoster of the neck, trunk, extremities, and ophthalmic area (herpes zoster ophthalmicus).   These latter forms of herpes have been shown to be identical in that they are associated with the same lesions of the nervous system (especially those of the sensory ganglion), and the changes in the skin are believed to be the same.

It seems further to have been conclusively demonstrated that the lesions of the skin are secondary to the primary changes in the corresponding sensory ganglia, which in turn may be brought about by a variety of causes.   The cases, however, may be classified into the primary or spontaneous herpes zoster, in which the affection is apparently primary and not due to any evident preceding infection or injury, and the secondary form, in which there is more or less clear evidence that the disease occurs as the sequel or complication of some antecedent affection, as pneumonia, cerebro-spinal meningitis, etc., or to injury.

Our knowledge of the changes in the skin in the various clinical forms of herpes is far from satisfactory.   Not until a sufficient number of careful observations upon the histological changes in all the stages of each variety of herpes is available will we be in a position to compare critically the processes, and, perhaps, distinguish clearly the different forms.   Suffice it to say for the present, that after comparing the histological appearances described by various authors of the changes in herpes zoster, herpes labialis and genitalis (all available), with some of my own cases herewith reported, and making due allowances for the different stages of the processes studied, I am not able to find any constant distinguishing characters by which the skin lesions of the various clinical forms of herpes may be separated.

I have recently had the opportunity of studying two cases which

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[1] Reference Handbook of the Medical Sciences, 1902, vol. iv.

throw some light upon several points of importance in the pathology of herpes. The first case occurred in the private practice of my friend Dr. Edward F. Cushing, who recognized its interest and importance and obtained the autopsy. I take this opportunity of expressing my thanks to Dr. Cushing for the autopsy and for the use of the clinical history of the case. This case illustrates the causal relation between acute infections and herpes zoster, and emphasizes the identity of the lesions of the skin and nervous system in primary and secondary herpes of the trunk.

CASE I. *Summary.* Bronchitis, acute croupous pneumonia of both lungs, herpes zoster of the left side, distributed on the back and side (sixth dorsal), and the abdomen (eleventh dorsal); congestion and hemorrhage into the capsular and interstitial tissue at one side of the eleventh dorsal ganglion, with slight cellular infiltration and destruction of a few ganglion cells; amylaceous and hyaloid bodies in another portion of the same ganglion. Slight chronic and acute interstitial nephritis, acute parenchymatous and interstitial hepatitis, acute splenic tumor, old pericardial adhesions, hypertrophy and dilatation of the heart; fibromyoma uteri.

*Clinical History.* Miss T., aged sixty-three years, had not been well for about one year. On October 10, 1901, she was taken sick with a cold in the head, which a few days later was followed by bronchitis. She then developed pneumonia of the lower lobe of the left lung. Later the whole of the left lung became consolidated. On the morning of October 24th there were the physical signs of consolidation of the lower lobe of the right lung. Coincidently with the consolidation of the lower lobe of the left lung there developed well-marked herpes zoster in the mid-dorsal region of the left side, extending from the middle line in the back to about the anterior axillary line, corresponding to Head's sixth dorsal area. During the last two days of life a similar eruption occurred on the abdomen, in the left umbilical and iliac regions (eleventh dorsal area; see autopsy protocol). Albumin was present in the urine. Death took place at 2.30 P.M., October 24, 1901. Autopsy six hours later. The autopsy was done hurriedly and under difficulties, at the home of the patient. The body measured 160 cm. long, was sparely built, except over the abdomen and lower portion of the back, where there was a considerable amount of fat. The body was cold, rigor mortis moderate. There were a few reddish discolored areas on the outer aspects of the legs. On the left side of the abdomen, situated in the outer and lower portion of the left umbilical and the upper portion of the left iliac regions there was an area, the size of the palm of the hand, studded with scattered pale-red or gray areas from 3 to 6 or 10 mm. in diameter. Some of these areas were elevated and covered with dry grayish-red material, while others showed a distinct loss of epidermis. No typical vesicles containing fluid were to be found, but the areas had the appearance of dried vesicles. In distribution this area corresponded with Head's eleventh dorsal area. A similar but narrow area extended from the middle line in the mid-dorsal region as far as the anterior axillary line under the nipple,

corresponding to Head's sixth dorsal area. The areas here were larger and the process appeared older than that on the abdomen. No other lesions were found upon the surface of the body. There was no facial herpes.

*Chest.* The chest was fairly well shaped, the muscles and fat rather wasted.

Both pleuræ were free from adhesions, and the pleural cavities contained no fluid. The visceral pleuræ over considerable areas were covered with a thin layer of fibrin, and were red and lustreless.

*Right Lung.* The apex was free from puckering and thickening. The upper lobe on section was congested and markedly œdematous. The whole of the middle and a large part of the lower lobe were consolidated, airless, and of a grayish-red color, and granular appearance. The mucous membrane of the bronchi was congested.

*Left Lung.* The whole lung was consolidated, airless, of a gray or grayish-red color, and granular appearance. The bronchial mucosa was congested. The bronchial glands were pigmented, but free from tubercle.

*Heart.* The pericardium was adherent to the diaphragm over a large area. Firm fibrous adhesions obliterated the pericardial sac. The walls of both ventricles were thickened. The valves, the coronary arteries and veins, as well as the aorta and large arteries, were normal. The myocardium was pale, otherwise normal; the heart weighed 400 grammes.

*Abdomen.* The muscles and fat of the abdominal wall were of ordinary appearance. The left lumbar region was prominent. The stomach was distended with gas, the large and small intestines contracted.

*Liver.* The liver was of ordinary appearance and size. The edges were rounded, the surfaces smooth, consistency not increased. On section the lobules are visible, the surface pale. The gall-bladder and bile-ducts were negative.

*Spleen.* The spleen was twice the ordinary size. On section it was of a grayish-red color; the trabeculæ and Malpighian bodies visible; consistency decreased.

*Kidneys.* The kidneys were of about the same size and appearance. The capsules were adherent in places, the surfaces were somewhat granular and marked by a few old scars. On section the consistency was somewhat increased, the surfaces pale, the cortices thinner than ordinary. The arteries, pelvis, ureters, bladder, and adrenals appeared normal, as did the stomach and intestines.

The ovaries were small and tough to the touch. The uterus was considerably enlarged; the body was the seat of a globular fibroma the size of an orange.

*Nervous System.* The brain could not be examined, and the examination was confined to the lower portion of the spinal cord; from the tenth dorsal segment downward with the cord the eleventh and twelfth dorsal and first lumbar posterior ganglia of both sides were removed. It was not possible to go higher in the time available for the examination. There was an excess of cerebro-spinal fluid, which, however, was quite clear. The meninges were normal in appearance. The cord showed no lesions on section. The ganglia showed no macroscopic lesions, and no hemorrhages were found about the posterior roots or the nerves going from the ganglia.

Portions of the various organs, including the cord and the ganglia, were hardened in Orth's fluid. The ganglia were transferred to 96 per cent. alcohol after a few hours. Portions of various organs, including the skin, were also hardened in Zenker's fluid.

*Bacteriological Examination.* Cover-slip preparations from the lungs and pleuræ showed lanceolate diplococci in capsules. Cultures on blood serum and on glycerin agar from the lungs, heart's blood, liver, spleen, kidneys, and cerebro-spinal fluid remained sterile.

*Histological Examination. Lungs.* Sections from both lungs showed well-marked croupous pneumonia, with lanceolate diplococci in the alveolar exudate.

*Liver.* There was well-marked fatty degeneration of the liver cells, congestion of the capillaries, with marked round-cell infiltration about many of the portal systems. No focal necrosis and no bacteria were found in suitably stained sections.

*Kidneys.* There were scattered areas of chronic glomerulitis, with thickening of the capillaries and of Bowman's capsule, with but little atrophy of the neighboring tubules. The epithelial cells of the convoluted tubules showed cloudy swelling. With no apparent relation with changes in the glomeruli or tubules, there were numerous areas of round-cell infiltration ; most of these cells were of the plasma-cell type, but some were lymphocytes. There was no necrosis of the renal epithelium and no abscess formation. No bacteria were to be found.

*Skin.* Sections were made through both areas of herpes, and, with the exception that the lesions were more extensive in the older lesion (sixth dorsal region), the changes were the same. There were few unbroken vesicles, but in most places the surface of the lesion was covered with amorphous and fibrillated fibrin containing a larger or smaller number of desquamated, swollen, and often disintegrating and necrotic epithelial cells. Some of these cells had undergone coagulation, and others liquefactive necrosis. In some places the cells of the deeper layer of the epidermis were markedly swollen, vacuolated, and evidently dropsical. In the fibrin and among the epithelial cells on the surface there were variable, often great, numbers of polymorphonuclear neutrophilic leucocytes. In some places there were cavities formed by the elevation of the superficial or subcorneal layer of epithelium. These were of considerable size in places, but were not numerous. Other small vesicles occurred in the exudate, their walls being formed by necrotic cells. Still other vesicles were between the epidermis and the underlying papillary layer. These were always small. In many places the papillary layer was exposed by the total destruction of the epidermis, and was covered by the exudation. In the papillæ and in the upper layer of the corium the veins and capillaries were markedly dilated, and in places there was hemorrhage, either into the tissue or upon the surface.

The papillæ and the upper layers of the corium showed other intense changes, coagulation necrosis, with hyaline and fibrinoid changes, nuclear fragmentation, and infiltration, with large numbers of polymorphonuclear neutrophiles, lymphocytes, and some plasma cells. Here and there a few eosinophiles were to be seen. This cellular infiltration was both diffuse and along the bloodvessels. Many of the sweat glands and hair follicles were swollen and distended with leucocytic and serous exudate. The epithelial cells were commonly swollen,

granular, and often desquamated and necrotic. About many of these glands there was well-marked leucocytic infiltration, a few of the cells being eosinophiles. Scattered collections of leucocytes were also seen in the deeper layers of the skin. No bacteria were to be found in any of the lesions in sections stained by Weigert's fibrin method or with eosin and methylene blue.

The whole appearance of the lesion points to rapidly necrotic and exudative processes.

*Posterior Root Ganglia.* Sections were cut of the eleventh and twelfth dorsal and first lumbar ganglia of both sides and stained by Nissl's, Weigert's, and Marchi's methods, as well as with methylene blue and eosin, and hæmatoxylin and eosin. Sections from all the ganglia studied, except the eleventh dorsal of the left side, were entirely normal.

In sections of the latter ganglion changes were found in two places: (1) at one side of the ganglion about midway of its length, and (2) at the peripheral end.

1. In the sections cut transversely through about the middle of the ganglion at one side there was considerable hemorrhage, with pigmentation, into the capsule. In some of the sections corresponding to the area of capsular hemorrhage there was just beneath the capsule marked congestion of the capillaries and interstitial hemorrhage between the ganglion cells. In several sections small areas of cellular infiltration about destroyed ganglion cells were found. The ganglion cells elsewhere stained well and appeared normal.

2. At the peripheral end of the ganglion there were a number of amylaceous and hyaloid bodies, both singly and in groups, of the size and shape of ganglion cells, and lying in spaces similar to ganglion cell spaces. Many of these bodies were finely granular, some of the granules staining pink with eosin, and others blue with toluidin blue. Many bodies stained diffusely pink with eosin, and some diffusely blue with blue dyes. In some a central nucleus was apparent, and many showed a concentric arrangement. In a few places hyaline masses were made out in lymph spaces and in blood capillaries. Hyaloid and amylaceous bodies were also found in unmistakable lymph and blood-vessels. The question whether or not some at least of these bodies represented degenerated nerve cells is difficult to answer. From careful study I am convinced that some of them were formed and lie in nerve cell spaces. No lesions of the peripheral nerve, the posterior nerve roots, or in the spinal cord, could be made out.

The interpretation of the pathological changes of the above case appear to be as follows:

Acute croupous pneumonia following bronchitis, with the ordinary parenchymatous changes of the liver and kidneys common in such cases, with the addition of acute interstitial hepatitis and nephritis; an herpetic eruption of certain cutaneous areas, the spinal root ganglion corresponding to one of which areas was shown to be the seat of definite lesions (congestion and hemorrhage of both the capsule and a small area of the interstitial tissue of the ganglion, with cellular infiltration about a few degenerated ganglion cells, with hyaloid and amylaceous bodies, in another portion of the ganglion).

It seems fair, in the light of our present knowledge, to attribute these various lesions to the toxins of the pneumococcus.

The failure to find degenerative changes in the cord, the posterior roots, and the peripheral nerve is in accord with observations of Head and Carpenter, who did not find changes in these organs in a case of herpes dying on the eighth day. They were present in a case dying on the thirteenth day.

Including the 5 cases of Lesser, Chaudelux, and Dubler with the 16 cases of Head and Carpenter, there are 21 well-studied cases of herpes zoster of the trunk in which definite destructive lesions have been demonstrated in the posterior root ganglia, corresponding to the distribution of the herpetic eruption. Two of the 21 cases of Head and Carpenter involved the head, in 1 case the ganglion was not removed, and in 2 others, in which death took place in 139 and 240 days, respectively, no lesions of the nervous system were found. In all 9 of the acute cases (three to sixteen days after the appearance of the eruption), definite and unmistakable ganglionic lesions were found. Of these cases 2 had had acute infections (cystitis, with retention of urine in paraplegia, and acute bronchitis and tubercular pneumonia). In the 12 chronic cases in which death occurred in from 57 to 790 days after the herpes the sensory ganglia corresponding to the distribution of the eruption showed well-marked chronic changes.

Our next case shows that the changes in the skin and Gasserian ganglion in herpes of the lips and nose in pneumonia are identical with those occurring in herpes ophthalmicus, and in the skin and posterior root ganglia in both primary and secondary herpes zoster of the trunk. It is also, curiously enough, apparently the first case of herpes of this region in which changes have been sought for in the Gasserian ganglion.

CASE II. *Summary.* Acute croupous pneumonia in a bartender, aged forty-one years. Death on the sixth day of the disease. Two days before death well-marked herpes of the upper lip and the nose, being much more extensive on the left side.

*Autopsy* showed acute croupous pneumonia (gray hepatization) involving the whole of the right lung, with fibrinopurulent pleurisy of the left side, œdema and congestion of the left lung. Chronic fibrous obliterative pleurisy of the right side. Herpes of the upper lip and nose, most marked on the left side. Congestion of the veins about the origins of the superior maxillary branches of both Gasserian ganglia. Hemorrhage into the capsule and tissue, with interstitial cellular infiltration and compression and degeneration of the ganglion cells near the origin of the superior maxillary branch of the left Gasserian ganglion. A few small areas of cellular infiltration in the same part of the right Gasserian ganglion. Marked congestion of the veins of the neck and brain and of the cerebral sinuses. Pneumococcus in the right lung and left pleura.

*Clinical History.* For permission to use the clinical history of the following case I am indebted to the courtesy of my colleague, Dr. J. H. Lowman, in whose service in the Lakeside Hospital the patient was admitted February 6, 1902, complaining of pain in the right side of the chest, cough, and fever.

The patient was a male, aged forty-one years, white, and a barkeeper by occupation. His family history was without present interest.

*Personal History.* He did not recall having ever been sick before, and denied having had diphtheria, scarlatina, rheumatism, pneumonia, pleurisy, syphilis, gonorrhœa, typhoid and malarial fevers. Some time ago he injured his right temple by a fall, but the wound healed promptly and was followed by no clinical symptoms. He drank beer and whiskey to excess at times, and also used tobacco. He had been a barkeeper for twelve years.

*Present Illness.* He got his feet wet on the night of February 8th, and awoke the next morning with severe pain in the right side of the chest, but did not have a chill.

On admission he had the physical signs of consolidation of the lower portion of the right lung. The left lung was clear. The spleen was enlarged. Examination of the other organs was negative. The leucocyte count on February 8th was 19,000, and on February 9th 13,000 per cubic millimetre. On February 9th, the fourth day of the disease, there appeared a well-marked vesicular eruption over the upper lip and the outer surface, and in the vestibule of the left side of the nose. This eruption on the lip and the outside of the nose extended somewhat to the right side of the median line. The sputum contained lanceolate diplococci. By February 11th the whole right lung was consolidated, and numerous moist râles were to be heard over the left lung.

The patient was delirious. Death occurred suddenly at 1.15 P.M., February 11, 1902, on the fifth day of the pneumonia and the beginning of the third day of the herpetic eruption.

*Autopsy One Hour after Death.* Body warm, no rigor mortis. Body 165 centimetres long, well built, and well nourished. There were no marks, scars, or wounds on the body. On the upper lip, involving both mucous and skin surfaces, there were a number of dried crusts surmounting slightly elevated areas, with red margins. These areas varied from 2 to 5 millimetres in diameter. Similar papules and dried vesicles were present on the skin of the vestibule and external surface of the left side of the nose. Altogether there were from fifteen to twenty such areas. Several similar lesions were also found to the right side of the median line of the lip and nose. No other herpetic eruptions were to be found on the body.

*Nervous System.* The veins of the dura and pia arachnoid and all the sinuses were markedly congested; the pia arachnoid was smooth and glistening. The structures at the base of the brain were normal. The brain on section showed congestion, but was otherwise normal in appearance.

*The Gasserian Ganglia.* The veins near the ganglion were engorged with blood. The ganglion was of ordinary size. On the upper surface just below the entrance of the sensory root and between and about the exit of the ophthalmic and superior maxillary branches the veins were congested and stood out prominently. The same appearance was seen on the posterior surface, but the congestion was less well marked.

*The Left Ganglion.* The vessels about the ganglion were engorged, as were the veins about and between the origin of the ophthalmic and superior maxillary branches of the ganglion. About the root of the superior maxillary branch this was very marked, and there was also hemorrhage into the capsule at this part on the posterior aspect of the ganglion. The fifth nerve and the branches from both ganglia appeared normal. The cord and the posterior root ganglia were not removed.

*Chest.* The chest was well formed; the sternum, ribs, and costal cartilages were normal.

The right lung was bound down by old but thin adhesions; the pleural cavity was obliterated. The right lung was consolidated throughout. On section it was firm and airless, of a grayish color, and quite granular in appearance. The mucosa of the bronchi was congested, otherwise normal. The left pleural cavity contained about 100 c.c. of seropurulent fluid. The surface of the lower lobe was covered with a thin fibrinous exudate. The lung crepitated throughout. On section the lung was markedly congested and œdematous, but was free from consolidation.

The description of the other organs is without present interest, and will, therefore, be omitted.

Cover-slips from the right lung and left pleura showed encapsulated lanceolate diplococci.

Plate cultures from both lungs, the left pleura, and heart's blood and pericardium showed pneumococcus in pure culture. Similar cultures from the liver, spleen, kidneys, and gall-bladder remained sterile.

*Histological Examination. Lungs.* Sections of the consolidated area showed well-marked croupous pneumonia, with lanceolate diplococci in the exudate. Sections of the other organs, with the exception of the skin of the lip and nose and of the Gasserian ganglia, showed nothing of present interest.

*Skin of Lip and Nose.* Bits of tissue were cut out and hardened in formalin and 95 per cent. alcohol, and sections were stained in carbol-toluidin blue and eosin, hæmatoxylin and eosin, and by Weigert's fibrin method.

The changes found were practically identical with those from the herpetic areas of Case I.

As in Case I., few well-developed vesicles remained, the surface of the lesions, as a rule, being covered with a crust of amorphous and fibrillated fibrin and fibrinoid material containing desquamated and often necrotic epithelial cells, polymorphonuclear and mononuclear leucocytes, and cellular and nuclear fragments. Here and there rather small vesicles could be made out. As in Case I., some were elongated cavities in the exudate, or in the superficial layer of the skin, just beneath the horny layer, while others were between the underlying inflamed papillæ and the epidermis. Most of the latter cavities were small, and their walls were formed of necrotic epithelium and their floors of the naked papillæ. In some places ballooning of the cells of the epidermis could be made out. In many places the margin between the necrotic and the unchanged epidermis was rather clear cut, but in some places near the necrotic portions the small vesicles could be made out in the neighboring otherwise normal epidermis. In most places at the site of the lesion the whole thickness of the epidermis was necrotic.

Beneath the fibrinous layer there were, in all sections examined, changes in the epithelium, marked coagulation and liquefactive necrosis, and hyaline transformation of the cells. The papillary layer and outer part of the corium were similarly affected. There was, in many places, marked nuclear fragmentation. The epithelium of the sweat glands and some of the hair follicles, when present, showed changes— swelling and liquefaction, and often a reticular appearance. Some cells were markedly swollen, many cells showed coagulation necrosis. Many nuclear fragments were to be seen. The bloodvessels, especially the capillaries and small veins of the papillæ and corium, were markedly dilated. Some were crowded with leucocytes. In some of the superficial vessels there were thrombi composed of pink-staining material. The papillæ and the superficial portions of the corium were diffusely infiltrated with great numbers of polymorphonuclear, neutrophilic, and large and small mononuclear leucocytes, and some plasma cells. The leucocytic infiltration could also be traced along some of the small vessels into the deeper layers of the corium. About some of the superficial veins and capillaries often large numbers of red blood cells had escaped into the tissue. Some of the lymph spaces were dilated. The lesions here, as in the herpes of Case I., were both degenerative and exudative, and involved both epidermis and corium. No inflammatory changes were found in nerves in the skin. No bacteria were found in the lesions of the skin, but in the superficial part of the fibrinous exudate, in sections taken from the vestibule of the nose, diplococci and some bacilli, morphologically like B. mucosus capsulatus, were found.

*Gasserian Ganglia.* The ganglia with the fifth nerve roots and the origins of the ganglionic branches were hardened in formalin (10 per cent. solution).

The two ganglia were mounted in celloidin, side by side, on the same block and cut in serial sections, every other section being stained and mounted in order. Many of the alternate sections were also stained.

In mounting on the block the left ganglion was at a somewhat higher level than the right, so in the parallel sections as mounted for histological study the two ganglia were not identical in structure, but as the series was followed to the end the right ganglion was found to be similar to the left in structural detail.

*Left Gasserian Ganglion.* In sections 1 to 8 there were no ganglion cells near the superior maxillary branch. The veins about this branch were enormously dilated and filled with red blood cells. In some places in the largest vein there were collections of leucocytes and larger and smaller granular masses, suggesting fibrin. No changes were found in the opposite end of the ganglion. About the dilated veins there was hemorrhage into the pia or capsule of the ganglion. In section 9 a small oval bit of ganglion tissue, containing ganglion cells, became apparent near the superior maxillary branch. In sections 9, 10, 11, and 12, corresponding to this, there were capsular and subcapsular hemorrhage, with compression of the superficial ganglion cells. In sections 15 to 35 the small strip of ganglion tissue in relation with the superior maxillary branch became very much larger, and formed an elongated strip of tissue traversing the thin portion of the ganglion, reaching from the side of the superior maxillary branch to, but not

uniting with, the larger ganglionic mass corresponding to the origin of the inferior or third branch.   About the middle of this strip there was marked congestion of the veins about the superior maxillary branch, into and, here and there, just beneath the capsule of the ganglion. This congestion and hemorrhage must have compressed the ganglion cells in this region.   Sections 36 and 37 showed the first well-marked changes in ganglion cells and interstitial tissue.   About the central portion of this strip of ganglion tissue some of the ganglion cells were vacuolated, others were very pale, non-granular, homogeneous, and stained poorly.   The nuclei showed no special changes.   Some ganglion cells were evidently necrotic, the cytoplasm staining diffusely, and the nuclei being displaced to one side.   Here, especially about the changed ganglion cells, there was marked cellular infiltration, with plasma cells, lymphocytes, and polymorphonuclear neutrophiles.

These cells were both in the interstitial tissue and grouped about changed ganglion cells, which were evidently compressed thereby.   In places there had evidently been a proliferation of the endothelial cells about the ganglion cells.

In sections 40 to 60 the congestion and hemorrhage were noticeable, the cellular infiltration being inconspicuous.

Beginning in section 73, cellular infiltration became marked again. In section 77, in the above-mentioned strip of ganglion tissue involving an area of from twenty to twenty-five ganglion cells, there was marked cellular infiltration with interstitial hemorrhage.   Some of the ganglion cells were necrotic.   Smaller areas of interstitial cellular infiltration were found near this area.

Section 78, showed, at the border of the same hemorrhagic area a group of degenerated ganglion cells surrounded by large numbers of lymphocytes, plasma cells, and polymorphonuclear leucocytes, red blood cells, and proliferated endothelial cells of the pericellular spaces.   The ganglion cells of the affected area showed the same changes described above; many have entirely disappeared.   They seemed to have been compressed and destroyed by the interstitial exudate and hemorrhage. A few ganglion cells in this area were the seat of large vacuoles. Nuclear figures could be made out here and there in the cells of the interstitial infiltration.   In most of the sections from 60 to 85 these changes were more or less well marked.   The area of hemorrhage could be traced in them all.   The changes in the left ganglion were lost after the 95th section.

*Right Gasserian Ganglion.*   All the sections cut showed congestion of the veins and capillaries about the second or superior maxillary branch, as described for the right ganglion.   Hemorrhage was, however, absent.   In sections 80 to 95 a few areas of cellular infiltration were found in the area corresponding to that showing similar changes in the left ganglion.

These areas of cellular infiltration were small and scattered, and nothing like so well marked as those found in the left ganglion.   In both ganglia a considerable number of amylaceous and hyaloid bodies were found in the lymph spaces.

In preparations of the fifth nerve, and of the superior maxillary branches of both sides, made by Marchi's method, no degenerations were to be found.

No bacteria were found in the ganglia or in the dilated veins.

That herpes zoster, following some part of the distribution of the trigeminal nerve is due to changes in the Gasserian ganglion is supported by observations on four previous cases.

Wys, in 1871 (quoted by Head and Carpenter), reported a case of herpes zoster involving the distribution of the whole of the first division of the trigeminal nerve ; the patient died on the seventh day of the eruption. There were thrombosis of the ophthalmic vein, abscesses of the eye muscles, and purulent infiltration of the connective tissue of the eyeball. There was hemorrhage about the origin of the ophthalmic division and about the inner side of the ganglion. Microscopically, there was extravasation of blood into the ganglion and into the first division of the nerve, with purulent inflammation of the ganglion.

Sattler, in 1875 (quoted by Head and Carpenter), reported a case of herpes ophthalmicus of the right side, in a man, aged eighty-five years, occurring some days after carbonic oxide gas poisoning. Death occurred fourteen days afterward. In the corresponding Gasserian ganglion there was destruction of ganglion cells and small-cell infiltration. The ophthalmic branch of the nerve showed degeneration, the other branches being normal.

Head and Carpenter reported a case of herpes of the right frontal region in which, one hundred and ninety days later, at autopsy, they found hemorrhage and destruction of ganglion cells in the right Gasserian ganglion.

In another case these authors studied the right Gasserian ganglion thirty days after an attack of herpes of the chin and cheek of the right side of the face (third division). " In that portion of the right ganglion which receives the fibres of the inferior maxillary branch of the nerve " there was congestion of the bloodvessels, destruction of ganglion cells, and cellular infiltration. Degenerated fibres were found in the fifth nerve central to the ganglion, in the pons and medulla, as well as in the inferior maxillary division of the fifth nerve.

Both of the last two cases were subjects of general paralysis. Wys' case was apparently spontaneous, while that of Sattler followed carbonic oxide gas poisoning. As far as I am able to find, these comprise all the observations on the relation between changes in the Gasserian ganglia and herpes distributed along the course of the trigeminus. Of these four cases, three were examples of ophthalmic herpes, and one of inferior maxillary herpes. I am not aware that the relation of the changes in the Gasserian ganglia to herpes of the upper lip and nose, occurring either spontaneously or in the course of pneumonia, malaria, cerebro-spinal meningitis, gastro-intestinal disorders, and other infections and intoxications, has been investigated.

I wish to call attention to the practical identity of both the lesions of the skin and of the nervous system in these two cases of herpes, the

one of the trunk, and the other of the upper lip and nose, both occurring during the course of acute croupous pneumonia. Reference to the detailed descriptions will, I think, show that the lesions agree in all important particulars, and only differ in severity. The extent and severity of the skin lesions are also in definite relation to those of the corresponding ganglia. The skin and ganglion changes in Case II. (trigeminal distribution) were more severe than in Case I. (dorsal 11). One is forced to the conclusion that the herpes of the trunk and the herpes of the lip and nose occurring in these two cases are identical clinically, histologically, and probably etiologically. They further demonstrate that the ganglionic lesions of herpes zoster of the trunk and herpes of the lip and nose occurring in pneumonia are identical with those described by previous observers for herpes zoster of the trunk and extremities and herpes distributed along both the first and third divisions of the trigeminus, occurring both spontaneously (idiopathic herpes), and secondarily to acute infections, as cystitis, bronchitis, acute tubercular pneumonia (Head and Carpenter), after poisons, as carbonic oxide gas (Sattler), and the invasion of tumors (Head and Carpenter). As far as I have been able to learn, no anatomical studies have been made on the lesions of the nervous system in herpes of the lip and nose occurring in malaria and other continued fevers, in pneumonia, cerebro-spinal meningitis, coryza, or gastro-intestinal disorders. We are also without similar observations in genital herpes. In the case of the latter, however, Unna's description of the skin lesions, based on observations in three cases, is practically identical with his findings in a case of herpes labialis in an individual dead of a continued fever, with these lesions of our cases and with those found by Head and Carpenter and others in herpes zoster. Unna, however, found marked ballooning of the epithelial cells of herpes zoster (trunk ?), a condition not found by him in herpes genitalis and his one case of herpes labialis.

In our case of labial and nasal herpes, in some places the swelling and liquefaction of the epithelial cells, especially in the hair follicles, was better marked than in the case of herpes of the trunk. It seems likely that in a necrotic and exudative process passing rapidly through different stages the changes would not be uniform in the lesions of each and every case. All that can be said at present is that the skin lesions of our two cases are identical and agree with those described by most authors.

Though there are no previous observations on the relation of changes in the nervous system in herpes labialis and nasalis occurring in pneumonia, and none at all in malaria, for the third acute infectious process in which herpes is common there are some most interesting and suggestive data. I refer to epidemic cerebro-spinal meningitis. In their

monograph on this disease, Councilman, Mallory, and Wright[1] call attention to the frequent occurrence of herpes of both the lips and nose, and to the fact that it may appear on other parts of the face and even elsewhere on the body; and in the summary on page 163 they state that "in its (the infection) extension along the fifth nerve it produces an acute inflammation of the Gasserian ganglion, with destruction and degeneration of the nerve cells composing it." On page 114 they state that sections were made of the Gasserian ganglia in five cases and of the spinal ganglia in two. The Gasserian ganglia in acute cases were "infiltrated with pus, and masses of ganglion cells were often separated from their connection." There was more or less hemorrhage; some ganglion cells were small and some devoid of nuclei; some cells contained large vacuolar spaces. Diplococci were found in some sections. In the more chronic cases the amount of leucocytic infiltration was less, but there was marked proliferation of the interstitial tissue, and in one case there was œdema, with marked cellular infiltration, especially about the ganglion cells, lymphoid, epithelioid, and plasma cells being found. There was atrophy, often going on to complete necrosis of the cells (ganglion cells). The spinal ganglia were not equally affected, but all seemed somewhat swollen and œdematous. On microscopic examination much the same changes were found in these as in the Gasserian ganglia. Degenerative changes were, of course, to be found in the nerves. They also showed that these changes may occur rapidly, for purulent infiltration was observed in the ganglia of a goat twelve hours after inoculation of the diplococcus intracellularis meningitidis into the spinal cord.

On page 125 they state that in one case the herpetic vesicles on the lip were examined. In them there was extensive infiltration, with pus cells in the tissue around the vessels, and proliferation of the fixed cells of the tissue. No mention is made of the epithelium; no diplococci were found in the pus cells.

Unfortunately no statement is made concerning the presence or absence of herpes of either the head or the trunk in the cases showing lesions of the Gasserian and spinal ganglia. In the one case showing skin lesions (small, dark purplish spots on the trunk and extremities) coming to autopsy they found congestion and dilatation of the bloodvessels of the skin, with hemorrhage in places, and in some places proliferation of the cells about the vessels. In the centre of the hemorrhagic area there was some infiltration with pus cells, and in one place the upper layers of the epithelium were slightly elevated by the accumulation of pus cells beneath.

These observations furnish at least ample explanation for the occur-

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[1] Report of the State Board of Health of Massachusetts, 1898.

rence of herpes of both the head and trunk in meningitis. The influence of the changes in the ganglia upon the other changes in the skin are, of course, only conjectural.

ETIOLOGY OF HERPES. From what has gone before, it is evident that the lesions of the skin and nervous system of primary, or idiopathic, or spontaneous herpes zoster of the head, neck, trunk, and extremities are the same, as are also the same lesions in certain cases of herpes of the trunk and face (upper lip and nose) occurring in pneumonia (Howard), and similar lesions of the nervous system in herpes of the trunk occurring in acute cystitis in a man with paraplegia, acute bronchitis; pernicious anæmia in a patient who had taken arsenic, and after the invasion of a lymphosarcoma (Head and Carpenter), and finally in ophthalmic herpes after poisoning with carbonic oxide gas (Sattler).

Primary herpes zoster is regarded by Head and Carpenter, and by Van Harlingen[1] and others, as an acute specific infectious disease due to an unknown cause, having a selective affinity for certain sensory ganglia in which certain degenerative, destructive and often inflammatory lesions are produced. These lesions in some unknown way cause acute degenerative, exudative, and proliferative changes in the skin and mucous, and possibly serous, membranes corresponding to the nerve distribution of the affected ganglia. There is a considerable amount of evidence in favor of the hypothesis that there is an acute specific infectious process of this nature, but no convincing proof has been so far adduced in its support.

It must be further borne in mind that there is a large group of cases of herpes either following the action of known toxins (carbonic oxide gas and arsenic), the involvement of the ganglia by tumors, or occurring in the course of certain infections, as pneumonia, malarial and typhoid fevers, and cerebro-spinal meningitis (in which, as has been shown, there are often intense lesions of the sensory ganglia), in all of which the lesions, as far as is known, are identical. Herpes, like pneumonia, meningitis, and inflammation in general, is a pathological condition, with definite lesions, capable, however, of being excited by a variety of causes, and is not always produced by the same causes; an efficient cause being one producing compression, degeneration, or destruction of ganglion tissue. It is not improbable that the primary lesions are often due directly or indirectly to the soluble toxins of various micro-organisms. The special frequency of labial and nasal herpes, and of herpes of the head and face in general, in malaria, pneumonia, and cerebro-spinal meningitis, is readily explained. In the case of malaria the organisms in the circulating blood often accumulate in the brain, where the Gasserian ganglia may be readily affected by con-

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[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1902.

gestion, the action of toxines, or even by capillary thrombi of parasites. In pneumonia, the organisms or their toxines may locate in the ganglia. What, however, to my mind seems the most reasonable predisposing cause of the frequent occurrence of labial and nasal herpes in this disease is the marked passive congestion which is so often present. This was especially noticeable in Case II., in which there was marked congestion of not only the bloodvessels and sinuses of the brain and meninges, but of the vessels of and near the Gasserian ganglia themselves, and especially about the second division. This marked congestion, which favors hemorrhage, the action of the toxines, poisons, and organisms in the blood, and thrombosis, may probably of itself, by pressure and by interfering with nutrition of the ganglion cells, cause degeneration sufficient to excite the herpetic changes.

As Councilman, Mallory, and Wright have shown, in epidemic cerebro-spinal meningitis, the spinal sensory ganglia, and especially the Gasserian ganglia, are often the seat of extensive changes due to the extension of the infection along nerve sheaths to these ganglia.

There is, a priori, no reason why changes in these ganglia should not occur in bronchitis and pleurisy. There is also no reason why the peripheral lesion in herpes zoster should not affect the pleura, as suggested by Curtin, just as the same process is known to affect the mouth, cheek, and pharynx. We know nothing in regard to the relation of lesions of the nervous system to the so-called simple herpes (with which labial and nasal herpes of pneumonia, malaria, and epidemic cerebro-spinal meningitis have hitherto been included) of the face, especially of the lips and nose, occurring in coryza, gastro-intestinal disorders, and the herpes genitalis.

It is to be hoped that observations will be made on this point, and it is not impossible that some cases, at least, will fall in the class we have been considering.

The question why should the peripheral changes occur after the lesions of the nervous system found in herpes is a difficult one to answer. There is no evidence that the skin lesions are due to the local presence of parasites, infection with which is predisposed by the nerve lesions.

Head and Carpenter are " inclined to think that the trophic disturbances of the skin are an extreme form of activity of the same cells, disturbance of which by afferent impulses along the white ramus produces the hyperalgesia that accompanies visceral referred pain ;" but they " do not imagine that the eruption of herpes zoster is produced by disturbance of special trophic nerves, but by intense irritation of cells in the ganglion which normally subserves the function of pain, and more particularly that form of pain produced by afferent visceral impulses."

This is, however, far from explaining why irritation of these ganglion cells and nerve fibres causes a severe inflammatory process marked by intense vascular changes, cell destruction, exudation, and proliferation The presence of hyaline, granular, and apparently red blood cell thrombi in many of the dilated bloodvessels of the herpetic areas in my cases is of interest, and may account for the hemorrhage, but were hardly extensive enough to explain the necrosis. What was the origin of these thrombi? Were they associated with changes in the vascular endothelium due to nerve changes? Were the hemorrhage and exudation due, in part, to the increased permeability of the vessel walls, the result of loss of nerve control or nerve irritability? These are some of the questions awaiting solution.

CONCLUSIONS. 1. Herpes zoster is a pathological condition, like pneumonia, for instance, with definite lesions of certain sensory ganglia, sensory nerves, and the skin, capable of being excited by a variety of causes. It is probable that the primary ganglionic lesions are commonly due directly or indirectly to the soluble toxines of various micro-organisms. The skin lesions may be on the head, neck, trunk, or extremities, corresponding to the Gasserian and posterior root ganglia affected.

2. Various forms can be distinguished. a. Spontaneous or primary herpes, thought by Head and Carpenter, and others, to be a specific infectious disease, the specific causal agent of which has a special affinity for certain sensory ganglia (posterior spinal and Gasserian). b. Herpes occurring after certain definite toxic agents, as arsenic and carbonic oxide gas, etc. c. Herpes occurring in the course of certain acute infectious diseases, as pneumonia, cerebro-spinal meningitis, and probably of malarial and typhoid fevers. The lesions of the ganglia and of the skin in the above three forms are the same, and the processes, therefore, presumably identical. d. Herpes simplex, so-called, affecting the lips and nose in coryza, gastro-intestinal intoxications, etc., and genitals (herpes genitalis) has not been sufficiently investigated to be classified; no evidence exists for or against its connection with changes in the nervous system.

3. As far as changes in the skin in herpes are concerned, they are illustrations of particular forms of necrosis and inflammatory reaction, and, as in similar lesions in other organs, can probably be excited in a variety of ways.

4. Herpes should be classified according to its relation to changes in the nervous system, and to this end every possible opportunity should be embraced for extending our knowledge in this direction.

# ACTINOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM, WITH THE REPORT OF A CASE DUE TO AN UNIDENTIFIED MEMBER OF THE ACTINOMYCES GROUP.[*]

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The observation of an apparently primary abcess of the brain caused by a branching, intertwining, thread-like organism similar to those recently found in a variety of lesions, and commonly called streptothrix, but properly classed under the genus Actinomyces, led to a review of the literature of actinomycosis of the central nervous system.

Including mine, eighteen cases were found, and of these the nervous system was apparently affected primarily in five, and secondarily in thirteen. On comparison many of these are very similar to each other and to our own.

It is my intention in the present article to state the salient features of the cases in the literature, report my own case, call attention to the identity of so-called Streptothrix with Actinomyces and, finally, summarize our knowledge on the subject.

## I. PRIMARY ACTINOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM.

The first recorded is that of O. Bollinger[1] (1887), who reported the case of a woman aged twenty-six years, whose illness began about one year before death with headache, soon after which there was paralysis of left N. abducens. Six months later there was paralysis, with eczema, of the forearms, and about this time she gave birth to a vigorous boy. Headache persisted, and nineteen days before death there was double vision and changes were made out in the left retina. Death occurred in coma after convulsions. Diagnosis,

brain tumor. The lateral ventricles were enormously dilated, and the foramen of Monro and the third ventricle were distended by a growth the size of a hazelnut, with smooth surfaces, and of a bluish gray color. On section a mucoid, sticky fluid escaped. Microscopically the mass was composed of granulation tissue containing numerous typical colonies of actinomyces. No other focus of actinomycosis was to be found in the body. The woman is said to have had bad teeth.

Almquist[2] (1890) reported the case of an artilleryman who died after a two weeks' illness with cerebro-spinal meningitis. The autopsy was made twenty hours after death. Plate cultures made from the base of the brain and from the lateral ventricles gave colonies of a large micrococcus, B. proteus, and a single colony of a streptothrix. This organism grew well on gelatine, forming rather large convex hemispherical colonies and causing liquefaction of the medium. On agar there was a rapid luxuriant growth, with larger and smaller white crusts. In broth there was a flaky growth, with a thin surface crust. Microscopically there was a mycelium of unjoined threads with true and frequent branching. The threads averaged 0.5 $\mu$. in diameter and sometimes reached 100 $\mu$. in length. Air hyphæ which broke up into small cubical or oval cells appeared on the white crusts. Both cells and threads stained lightly with the aniline dyes. No mention is made of finding this organism in the pus or sections of the meninges, or of animal experiments. Absence of microscopical proof of the presence of this organism in the lesions and the fact that a single colony was obtained in the cultures lend strong probability to the natural inference of air contamination. I am, therefore, very strongly inclined to question the propriety of including this case.

In 1895 Ferré et Foquet[3] reported the case of abscess of the brain of a man who during life had epileptiform crises. From the description the brain abscess was probably primary. From the pus they obtained a "streptothrix" in pure culture. The organism grew well on the various media, but best on

potato. Microscopically it was made up of ramifying fila-
ments with knob-like terminations. The organism stained
by Gram and was not pathogenic for guinea-pigs. On sub-
dural inoculation of a rabbit there was general diffusion of
the parasite in the organs without reaction or the formation
of pseudo tubercles.

Musser, Pearce, and Gwyn[4] in 1901 reported a case of
probably primary brain abscess in a man twenty-four years
old. " At a point just posterior to the upper portion of the
fissure of Rolando is an area three centimeters in diameter
which is fluctuant, grayish yellow in color." The side of the
brain affected is not mentioned. On section at this point
there was found an abscess 3.5 cm. in diameter, containing
thick partly chocolate-colored and partly grayish yellow
fluid of the consistency of oil. No granules were made out.
The walls of the cavity were greenish gray in color and soft
and neurotic. The brain tissue about the abscess was softened
and of a yellow color. The pus had a foul odor. (The
striking resemblance to the abscess in my case will be noted.)
The rest of the brain was normal. The ears and the bones
of the skull appeared normal. The other organs could
not be examined. In the pus of the brain abscess after
search there was found a large ball-like tangled mass made
up of long irregularly staining filaments. There was some
suggestion of branching of the periphery of the mass. His-
tological examination of the abscess wall showed a large
mass of radiating threads, which at the periphery were long
and thin and stained irregularly. The whole had the appear-
ance of an actinomyces colony. Clubs and rosettes could
not be demonstrated. No tubercle bacilli could be found.
Aerobic and anaerobic cultures and animal inoculations
(guinea-pigs) were negative.

J. C.—Male, white, aged fifty-two years, was admitted to
the medical wards, service of Dr. Edward F. Cushing, of
the Lakeside Hospital, April 21, 1902. The patient had
been an orderly in the hospital for a number of years and
had always been well until his present illness. Several days
before his illness he had complained of not feeling well, and

for two days before admission to the ward he had not re-
ported for work. On the morning of April twenty-first he
was found in his room in a condition of stupor. He was
very drowsy, but on being aroused could answer questions
and complained of pain in his right eye. The conjunctiva of
this eye was reddened, the other pupil was markedly dilated.
The left eye and pupil appeared normal. The patient could
move his hands and arms and there was no evidence of
paralysis. His eyes were examined by Dr. Millikin, who
found nothing abnormal. Physical examination disclosed
nothing further except varicosity of the veins of the left leg.
Ulceration of the leg is not mentioned in the clinical history
and was therefore probably not present. On April twenty-
second his condition was much the same, but questions were
answered with difficulty and stupidly. The right pupil was
dilated and did not react to light. Breathing was regular
and somewhat accelerated. The pulse was full sixty-four to
the minute. Physical examination of the thorax and abdo-
men was negative. The knee jerks on both sides were much
increased. On the left side there was a marked Babinski re-
flex. The patient could move his upper and lower extremi-
ties, but there was marked rigidity of the muscles of the left
arm and to a less degree those of the left leg. The tempera-
ture ranged between 100° to 101.5° F. There was involun-
tary micturition and defecation. On April twenty-third the
note made records that the patient continued throughout the
preceding day in a comatose state, and during the night the
coma deepened. At times he was quite restless and com-
plained of pain in the right side of the head. To-day there
was deep coma from which he could not be aroused. The
right pupil was still widely dilated; the reflexes were the
same as yesterday. There was now rigidity of the right arm
and leg, with paralysis of the left arm and leg. Breathing
was stertorous, but not especially rapid. The pulse was
strong and eighty to the minute. The leucocyte count
showed twelve hundred per cubic millimeter. There was
no discharge from the ears, the membranes appeared normal.
He was transferred to the surgical service of Dr. Dudley P.

Allen, who trephined over the motor area of the right side. There was distinct bulging of the brain when the dura was cut through. The meningeal vessels were markedly congested, but no hemorrhage and meningitis, and no evidence of brain abscess were found. The rigidity of the arms became less marked after incision of the dura. The patient died at five-forty the afternoon of April twenty-third. Autopsy six hours after death. The body was fairly well built and nourished, and 170 cm. in length. Rigor mortis was present. The right side of the head was shaved and over the right parietal region there was a semicircular wound closed with sutures. The right pupil was somewhat larger than the left, which was of ordinary size. The external surface of the left leg was the seat of a large varicose ulcer. Near this there were a number of scars of former ulcers. No other scars were to be seen. The head was of ordinary size and shape. The wound above referred to was healthy in appearance and free from pus. The skull was of ordinary thickness and appearance. There was no softening. The dura at and near the seat of the operation was markedly congested. The brain and pia-arachnoid bulged slightly at the opening. The pia-arachnoid over a considerable area was congested and in a large vein just beneath the wound contained a dark red thrombus. On removal of the brain, the superior tempero-sphenoidal and the superior marginal convolutions of the right side were somewhat softer than usual. About the middle of the superior tempero-sphenoidal convolution and 15 mm. below the trephine hole through the skull there was an area of fluctuation just beneath the surface. On handling the brain it ruptured at this point with the escape of a considerable amount of dark, grayish green, thick pus with a foul putrid odor like that of butyric acid fermentation. On incision in this region there was an abscess the size of a walnut, surrounded by several smaller abscesses varying from 3 to 15 or 20 mm. in diameter. They all had soft necrotic walls and were evidently recent. The brain tissue for some distance, 4 cm. in some places, on all sides of the main abscess was soft, edematous, and of a peculiar gelatinous consistence

and appearance. The abscesses with the area of softening extended antero-posteriorly from the ascending frontal to the angular convolution and internally nearly to the right lateral ventricle. The pia-arachnoid over the abscess was markedly congested and cloudy in appearance. On section of the brain no other abscesses were to be found. The structures at the base and all the vessels appeared normal. The sinuses were free from thrombi and the middle ears and mastoid cells were normal.

The spinal cord was not removed.

Chest. The muscles were well developed; the costal cartilages were calcified. Both lungs were bound to the chest-wall by dense fibrous adhesions; both pleural cavities were almost completely obliterated. Both lungs were voluminous and on section markedly congested and edematous. No areas of consolidation were to be found. The bronchi contained frothy, blood-stained serum. The bronchial glands were pigmented, but otherwise were normal. The pulmonary vessels were normal. The trachea, tongue, and thyroid were negative. The heart, liver, kidneys,. spleen, stomach, intestines, and other organs showed nothing of present interest and their description is therefore omitted.

The thick, creamy, grayish green appearance and the butyric acid odor of the pus of the brain abscess reminded me at once of pus with similar characteristics obtained some years ago from two cases of empyema from which an organism apparently belonging to the ray fungus group was obtained, so cover-slips were examined immediately during the progress of the autopsy. The pus was rich in polymorphonuclear neutrophilic leucocytes and showed a few scattered bacillus and thread-like forms. In several preparations stained by Gram's method larger and smaller clumps of branching threads were found. A few leucocytes containing bacillus and long thread-like forms were seen in some preparations. The threads varied very much in length and to some degree in thickness. The bacillus and thread-like forms varied from three to thirty or forty microns in length. As a rule they stained deeply and uniformly with

fuchsin and gentian violet in either aqueous or aniline solution, but in many, especially the shorter forms, *i.e.*, those of four to eight microns · in length, showed larger or smaller unstained areas which usually involved the whole thickness of the organism. In some of these forms with unstained areas a thin cell membrane was discernible. The organisms varied from 0.3 to 0.5 in thickness, the former being the average. Some forms showed irregular slight swellings, which were usually situated at one or the other end. No typical knob or club-like forms could, however, be found. The ends were usually square, were often rounded, especially in the shorter forms. Many of the longer forms were wavy in outline. Some of the shorter forms were bent, forming almost comma shapes. Some threads and rods showed transverse division into short bacillus and even coccus forms, and thus chains of bacilli and cocci were not uncommon. The latter forms were always larger than streptococcus pyogenes. The mass of intertwining branching threads showed no special spore-bearing structures; careful search failed to demonstrate the presence of clubs. The forms were non-septate, and the branching was true, the protoplasm of the main stem always being directly traceable into the branches. In the larger clumps the growth was always radiating, and the mycelium formed a distinct felt work. No capsules could be made out.

Numerous cultures, both aerobic and anaerobic on slants and on Petri plates were made on various media, including plain glycerine and glucose agar and potato with glucose bouillon and chest serum, inoculated from the pus of the brain abscess. Care was taken to use a large amount of pus for sowing the cultures. In many of the cultures streptococci, which reacted in every way to the tests for streptococcus pyogenes, grew. In none of the cultures were there forms suggestive of those found on the coverslips. Following the plan of Norris and Larkin, attempts were made to grow the organism on the organs of newly killed rabbits, but · always without success. Aerobic plate cultures from the lungs gave streptococcus pyogenes and staphylococcus ·

pyogenes aureus (a few), from the liver and kidneys strepto-
coccus pyogenes.

A rabbit and a guinea-pig were inoculated at once intro-
peritoneally.

The guinea-pig remained well and was killed six weeks
later and showed no lesions.

The rabbit died twelve days after inoculation, and showed
a wide-spread purulent peritonitis, the peritoneal cavity being
distended with a large amount of thick, white, sticky pus of
the consistency of thick cream, with a well marked butyric
acid odor. The surfaces of the liver and spleen, as well as
those of the intestines, were covered with similar material.
Coverslips showed no branching forms, but numbers of long
and short threads, bacillus and coccus forms, with leucocytes.
Cultures from the peritoneum showed a few colonies of
streptococcus pyogenes, but no other organisms.

Pus from the peritoneal cavity was inoculated into the
pleural cavity of a rabbit (rabbit II.), which died in three
days with extensive purulent pleuritis and pericarditis, and
pus from this inoculated into a third rabbit (rabbit III.)
caused its death in two days with identical lesions.

Other rabbits were inoculated intravenously with pus from
the peritoneal cavity of rabbit II., died within a few minutes
with extensive thrombosis of the right ventricle, and one
inoculated into the trachea died during the night with puru-
lent pleuritis. . (Rabbit IV.)

Histological examination and sections from various por-
tions of the brain showed as follows:

Brain abscess : A number of sections cut in both celloidin
and paraffin and stained in hematoxylin and eosin, toloidin
blue and eosin, aniline oil gentian violet, followed by ani-
line oil and xylol, Weigert's gentian violet method, aniline oil
fuchsin followed or not with iodine, decolorized with aniline
oil, and Mallory's stain for clubs; Weigert's stain followed by
aniline fuchsin, and the Ziel stain for tubercle bacilli.

The abscess was made up of a thick mass of cells, most of
which were polymorphonuclear neutrophilic leucocytes, among

which there were both large and small mononuclear cells.
About the margins of the abscess the tissue was infiltrated
with the same varieties of cells, and often contained red blood
cells.   Many of the cells were necrotic; nuclear fragments
were numerous.   The brain tissue for a considerable distance
from the abscess proper was edematous, and contained col-
lections of leucocytes.   The blood vessels were markedly
dilated, and in many places there was marked perivascular
cellular infiltration, with proliferation of the endothelium of
the perivascular lymphatics.   No micro-organisms were
found in the blood or lymph vessels.   The only micro-organ-
isms to be found were clumps of long threads always lying
near the centre of small abscesses or about the margin of a
large abscess.   These organisms were sometimes seen singly
or in small clumps, but nearly always formed larger or smaller
colonies from twenty to one hundred microns in diameter.
These colonies were composed of branching nonseptate
threads, which formed a meshwork and radiated from the
centre of the colony.   These colonies when cut through the
centre were nearly round in outline and had often rather
regular but somewhat serrated margins.   In sections stained
with hematoxylin or methylene blue the colonies are finely
granular and stain homogeneously with the blue stain.   No
organisms were made out even at the periphery.

In very thin sections stained with eosin followed by Wei-
gert's fibrin stain, very beautiful pictures were given.   Here
the colonies appeared composed of a finely granular pink
ground, traversed by radiating, intertwining, branching dark
blue threads, which projected from the margin of the colony
in an irregular wavy line.   The finely granular structureless
pink staining mass appeared to support the mycelium of
branching threads.   The threads were usually more thickly
placed at the border of the colonies, and while on first exam-
ination the outlines of the colonies were uniform, closer study
showed that many threads projected for some distance from
the colonies between the surrounding leucocytes.   Hence the
relation between the colonies and the surrounding leucocytes
was an intimate one.   No leucocytes were ever, however,

found penetrating the colonies, although they approached individual threads. These projecting threads never formed clubs, and showed no special tendency to break up into short bacillus and coccus forms. Near the colonies both long and short free threads were to be found. Reverting to the threads in the colonies, they stained well with aniline gentian violet and both aniline and carbol fuchsin, and retained the stain tenaciously whether treated or not with Lugol's solution, or exposed to aniline oil or alcohol.

The threads were of about the same size as those described on coverslips made from the fresh pus. They often showed unstained spaces and irregular lateral swellings or bulging of the cell membrane. Many were wavy and tortuous in outline. The threads took the stain very differently — some deeply and others very faintly. No clubs were found. The threads were not septate. No spore-containing bodies were seen. Here and there among the leucocytes were larger and smaller masses of threads, some of which were evidently parts of colonies, while others represented detached masses. The threads readily yielded the fuchsin and gentian violet stains on treatment with acids in either weak aqueous or alcoholic solution, and therefore do not belong to the acid fast fungi.

Sections, including the pia-arachnoid, over the abscess and near the seat of operation, showed congestion of the blood vessels and leucocytic infiltration. No threads were found here. Histological examination of the other organs showed no acute or chronic lesions in any way suggestive of reaction to this fungus.

Animal experiments and sections of the peritoneum over the abdominal wall, liver, and intestines of rabbit I. showed swelling, desquamation, and necrosis of the endothelium in places, with an exudate of leucocytes. The leucocytic accumulation varied markedly in extent in different places. There was a notable absence of fibrin. Most of the leucocytes were of the polymorphonuclear neutrophilic type. Among the leucocytes there were in many places great

numbers of bacillus and streptococcus forms.  In some places long threads were seen, but no branching forms could be found.  The threads were never in the form of colonies, as in the brain abscess, but were met with singly or in scattered clumps.  They were of the same size, general appearance, and had the same staining characters as those described in the brain abscess.  The same applies for the bacillus and coccus forms.  Many of the former were curved or bent, and the latter were on the whole larger than streptococcus pyogenes.  No nodular formations were present in the peritoneum or in the organs.  Sections of the lungs and pleura and pericardium of rabbits II. and III. showed wide-spread purulent exudation, without recognizable fibrin, or the formation of definite nodules.  The micro-organisms were even more numerous in these exudations than that of rabbit I.  They had the same characters, with the exception that here clumps of definite branching forms could be found.  There were no well-marked colonies, but somewhat elongated tissues of interlacing threads, some of which showed true branching.  The shorter non-branching bacillus and coccus forms were, however, much more numerous.  In both animals, as in the brain abscess, there was a certain amount of phagocytosis on the part of the polymorphonuclear leucocytes, some of which contained numbers of short threads or forms.

The parenchyma of the lungs of rabbit II. was not appreciably affected, and no organisms were found in other organs.  The organisms had the same staining reaction noted for those in the brain abscess.*

Including Almquist's rather doubtful case, there are five known cases of primary cerebral actinomycosis, three of which have been reported as instances of "streptothrix" infections.  In all except Bollinger's case, the only one to show the changes of "typical actinomycosis," the course of the disease was acute.  In this case the diagnosis was brain tumor.  In one case the diagnosis was tuberculous meningitis,

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* My thanks are due to Drs. Cushing and Allen for the use of the clinical history of the case.

in another, cerebro-spinal meningitis, and in one cerebral hemorrhage. Four cases were males and one female; all were adults.

The organisms were cultivated in two cases (Almquist and Ferré et Fouquet), and not classified as typical actinomyces, but as " streptothrices."

Pathogenesis for animals was tried in four cases, and was positive in only one (mine).

## II. SECONDARY ACTINOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM.

The earliest reported case of secondary cerebral actinomycosis is that of Ponfick,[5] described in his work on actinomycosis in 1882, and quoted by O. Bollinger. A woman who had actinomycosis of the neck and prevertebral tissue developed actinomycotic masses of the left cerebral hemisphere, as well as of the pericardium, lungs, and spleen. In a second of Ponfick's cases, an actinomycotic process extended directly through the skull and invaded the pia and the right temporal and frontal lobes.

Kohler,[6] in 1884, reported the case of a man with a number of fluctuating nodules on the surface of the body which were mistaken for glanders. At autopsy there were found ulceration of the upper jaw and sternum, and abscesses of the brain, neck, tongue, spleen, liver, and kidneys, and colon. In the tenacious green pus of the various abscesses there were small greenish masses, which on microscopical examination proved to be colonies of a ray fungus. No mention is made of cultures or animal inoculations.

O. Israel,[7] in 1884, described the case of a laborer thirty-one years old. who entered the hospital with a number of ulcers and abscesses on the surface of the body. At autopsy there were found ulcers of the skin of the chest, pericardial adhesions, abscesses of the heart, spleen, liver, kidney, and intestine, and brain. Numbers of actinomyces were found in the pus from the skin lesions.

Naunyn,[8] in 1888, reported the case of a girl of sixteen years who died with the symptoms of chorea. At autopsy

there were small excrescences on the mitral valve and red-
dish-brown masses on the cerebral pia-mater.   In both
lesions a branching thread-like organism was found.   Cult-
ures and animal experiments were not mentioned and were
probably not made.   It is interesting to recall that Zopf, to
whom specimens were submitted, classified the organism as
a species between Cladothrix and Leptothrix.

Keller,[9] in 1890, reported the case of a female forty years
old who had pleurisy in 1885, and who in 1886 developed an
abscess over the sixth and seventh costal cartilages.   Acti-
nomyces were found in the pus of these abscesses.   Two
years later she was taken ill with convulsions, paralysis of the
left side, and coma.   At operation, and later at autopsy.,
chronic meningitis and a small abscess at the right side of
the brain were found.

In 1891 Eppinger[10] described, under the title " Ueber eine
neue pathogene Cladothrix und  eine durch sie hervorgeru-
fene Pseudotuberculosis (Cladothrichica)," a case of brain
abscess and meningitis associated with changes in the bron-
chial and supra-clavicular glands.   The patient was a glass-
worker, fifty-two years old, who developed what was appar-
ently joint rheumatism.   Eight days later he was unable to
work.   Later there was paralysis of the left side, tenderness
of the right side of the head, delirium, and coma.   Death
occurred after an illness of twelve days.   At the autopsy the
skull was healthy.   There was well-marked cortical, basal,
and spinal meningitis, the exudate at the base of the brain
being thick and sticky and of a yellow color.   The brain
tissue was congested and soft, the lateral ventricles were dis-
tended with yellowish pus.   Communicating with the right
lateral ventricle through an opening in the optic thalmus
there was a large abscess of the right hemisphere extending
from the middle of the frontal to the occipital lobe.   The
abscess was filled with pasty pus ; its wall was thick and
rather firm.   There were firm nodules in the lungs and
pleura (pseudo-tuberculosis).   The bronchial and mediasti-
nal lymph glands contained firm grayish-white nodules.   The
right supra-clavicular glands were very much enlarged and
soft.

In coverslips, and in cultures from the brain abscess, the meningeal exudate, and the bronchial and supra-clavicular lymph glands, Eppinger obtained a branching, thread-like organism growing in star-shaped colonies which produced pseudo-tuberculosis in both guinea-pigs and in rabbits. This organism, which grew readily on ordinary culture media, has been classed by Kruse, Lehmann, and Neumann and others as Streptothrix Eppingeri. MacCullum, who has recently isolated the same organism from a case of peritonitis, correctly classes it under the actinomyces, as Actinomyces asteroides.

Sabrazés et Riviere [11] (1894) described the case of a man thirty-one years old, an alcoholic, who was said to have been ill for three weeks before admission to the hospital. Ten days before admission he showed marked mental disturbance. The day of his admission he was aphasic, had great pain in the head, vomiting, and obstinate constipation. He soon became comatose and died.

Diagnosis, tuberculous meningitis.

At the autopsy the meninges were found normal. The left cerebral hemisphere was markedly edematous, soft, and almost diffluent. There was an abscess the size of a small orange in front of the centrum ovale in the prefrontal region and involving the first and second frontal convolutions. The apices of both lungs were consolidated and one contained a small abscess. The right kidney was the seat of a large infarct. In the green pus of the cerebral abscess there were long branching filaments, some showing unstained areas. Chains of irregular micrococcus-like forms were also seen. The same appearances were met with in the renal infarct, where coccus and rod forms as well as masses or colonies of interlacing filaments were also plentiful. The colonies were circular in shape and had a radiated appearance. The ends of the filaments were regular, and showed neither swelling nor diminution in size. Sections of the brain abscess showed edema and disintegration of the brain tissue, with inflammation; but no organisms were found. Sections of the renal infarct showed them, however. No filaments were found in

the lesions of the lungs. The organism failed to grow aerobically, but an anaerobic gelatine culture gave, after five days, a single colony of branching, filamentous organism like that found in the brain and kidney. Transplantation was unsuccessful. A guinea-pig inoculated with the pus from the brain died in two days of septicemia due to a micrococcus.

As no organisms were found in the pulmonary lesions, the portal of entry is obscure and the primary seat of the affection is uncertain. It is probable, however, that more careful investigation would have discovered the fungus in the lungs. The bronchial glands were not mentioned.

The authors regard their organisms and that of Eppinger as different from that of actinomycosis.

Dolore,[12] in 1896, recorded the case of cervical and facial actinomycosis with loss of consciousness, delirium, convulsions, and episthotonus. At autopsy there was found marked cerebro-spinal pachymeningitis, in the exudate of which there were yellow granules, which on microscopical examination proved to be actinomyces.

In the same year C. F. Martin[13] reported from Chiari's laboratory two cases of secondary actinomycotic abscesses of the brain. In the first, a man thirty-eight years old, with actinomycosis of the lungs, sternum, and ribs, there was a metastatic abscess of the left occipital lobe. Actinomyces were found in the pulmonary lesions, and in the pus of the cerebral abscess. In the second, a boy of sixteen years, there was actinomycosis of the right lung and chest wall, with metastatic abscesses of the right cerebral hemisphere, the right lung, and the kidneys. The secondary abscesses were acute and contained numbers of actinomyces, clubbed forms being rare. Yellow granules were visible in the pus of both the skin and the cerebral abscesses. No mention is made of cultures or animal experiments.

In 1900 Chiari,[14] under the title of "Ueber Myelitis suppurativa bei Bronchiektasie," recorded two cases of meningitis and abscesses of the central nervous system containing branching threads which he regards as identical with, or closely related to, actinomycosis. Both occurred in males

with bronchiectasis.   Sections of the bronchiectatic cavities which were made in one of the cases showed the same organisms found in the lesions of the nervous system ; hence Chiari regards the latter as secondary in both cases.

In the first, a man forty-three years old, there was a large abscess of the cerebellum, multiple abscesses of the cord, with cerebro-spinal meningitis.   In addition to Pneumococcus, bundles of branching threads without peripheral clubs were found in these lesions.   There was no growth in cultures after two days, and no animal inoculations were made.   The masses of threads were thin, showed true branching and took the various stains, including Gram's.   Club formation was not observed.   Chiari states that the organism of this case had the same microscopical appearances of those found in Martin's above described cases of secondary cerebral actinomycosis, in which the " drusen " of the cerebral abscesses lacked peripheral clubs, though the latter were present in the lesions in the other organs.

Chiari's second case was a man thirty-seven years of age who had chronic purulent bronchitis, with saccular bronchiectasis of the right lower lobe, purulent cerebro-spinal meningitis, with an abscess of the left frontal lobe.   The brain abscess and sections of the wall of the bronchiectatic cavities showed numerous bundles of branching threads similar to those found in the first case, with the exception that some threads showed peripheral clubs.

No cultures or animal inoculations were made.

### III.   CLASSIFICATION.

It is quite evident that the micro-organism found in my case does not belong to the lower bacteria on the one hand, and lacks some of the characters usually regarded as distinctive of the typical actinomyces on the other.   We have to deal with an organism which forms a mycelium of elongated branching, intertwining, or interwoven threads, which break into beaded segments forming chains of coccus and rod-like forms, but which apparently does not form clubs or club-shaped hyphæ.   It caused in rabbits diffuse suppuration in

the subcutaneous tissues and diffuse peritonitis without nodules and without typical mycelia, only long and short threads which sometimes branched, and coccus and bacillus forms being present in the exudates.  Failure of the organism to grow in artificial media and on the organs of freshly-killed rabbits interferes seriously with its comparison with somewhat similar organisms described as actinomyces, streptothrices, and psuedo-actinomyces.  The terms " cladothrix " and " leptothrix " clearly do not apply here, and the term " streptothrix," though used by Eppinger,[10] Ferré et Foquet,[3] Sobrases et Rivière,[12] Flexner,[15] Norris and Larkin,[16] Musser, Pierce, and Gwynn,[4] and others for organisms more or less closely corresponding to mine is a misnomer, as Lachner-Sandoval[17] and Hektoen[18] have clearly pointed out.

Kruse[19] and Lubarsch[20] are largely responsible for the application of the term " streptothrix " to the group. Lubarsch would include under the group name of streptothrix, placed midway between hyphomycetes and schizomycetes, all ray fungi, as well as those organisms usually classed as bacteria, which occasionally produce true branches in cultures and ray forms in the animal organism, regarding the various members of the group as transition stages.  As a distinct family of the streptothrix group, Lubarsch would separate those organisms which occur in ray form in the tissues, calling them ray fungi.

Hektoen[18] strenuously objects to the bringing together in a closed circle the most typical member of the group actinomyces albus, with the most atypical or imperfect, as the tuberculomyces, for instance, simply on the strength of what many in opposition to Lubarsch and others regard as a pathological condition, namely, club formation.

Hektoen further points out the illogical and untenable position of those who use in this connection the term " streptothrix," a term used by Corda in 1839 for an entirely different family of hypomycetes.  Hektoen, therefore, following the lead of Gasperini, Berestenew, and Lachner-Sandoval, insists, according to the principle of priority, upon the use of the term " actinomyces " for this group.  MacCallum[21] and Abbott and Gildersleeve[22] have recently emphasized this.

Lachner-Sandoval [20] recognizes twenty-nine species of ray fungi, and as some of these forms have not been cultivated on artificial media the group may be smaller, owing to unknown duplicates. Many new species must be added if the term is to include all the branching, mycelium and club forming organisms now classed as bacteria (the acid resisting bacilli, B. diphtheriæ, etc., see Abbott and Gildersleeve [22]).

Berestenew [23] concludes that the ray fungus disease, caused by parasites of genus actinomyces, to which various names such as streptothrix, oospora, nocardia, etc., have been given, may be divided into (*a*) typical actinomycosis (such as described by Bollinger and J. Israel Wolff, Boström, and others); (*b*) atypical actinomycosis without granules in the pus and without spherical masses of the parasites in the tissues, to which belong the cases of V. Eppinger, Sabrozes et Rivière, as well as certain cases of Berestenew and others; (*c*) pseudo-actinomycosis, that is, cases with all the symptoms of typical actinomycosis, and caused by different microorganisms, (1) those which stain by Gram and which like B. tuberculosis possess the property of forming branched threads with clubs, and (2) those caused by bacteria which do not stain by Gram's method. He describes several cases of psuedo-actinomycosis.

Silberschmidt, [24] writing in 1901, studied the organisms from seven cases of human and two of bovine actinomycosis. Of the human cases, one was unusual as involving the lungs, liver, and thigh, three were cases of infection of the lower lachrymal duct, and three were typical clinical cases of actinomycosis (jaw, mouth, and back). With the exception of two of the forms from the lachrymal duct, all showed great similarity in their cultural characters, but none corresponded morphologically with the form described by Boström as the only cause of human and bovine actinomycosis. There was great similarity to the forms described by Wolff and Israel, but there were many cultural differences.

Silberschmidt regards as similar to his the organisms from two of Berestenew's cases of so-called psuedo-actinomycosis.

He quotes Poncet and Berard's description of the points of difference between actinomycosis and pseudo-actinomycosis:

(1.) In actinomycosis the mycelium consists of hairlike, radiating threads with numerous peripheral clubs, while in pseudo-actinomycosis the mycelium is more interlaced or interwoven and not radially arranged, the branching less frequent, and the spores " lightly stained," the organism having more the appearance of leptothrix.

(2.) The actinomycosis fungus is more difficult to cultivate and may be either aerobie or anaerobic, while in pseudo-actinomycosis the growth is more luxuriant and microscopically made up mostly of forms like B. diphtheria, but with neither granules nor long threads.

After comparing the cultures from his own cases with each other and with others obtained from l'Institute Pasteur and Krâl's laboratory, Silberschmidt makes the following groups:

(1.) Growth aerobic and at room temperature, colonies on agar and blood serum are adherent to and send out numerous mycelial outgrowths into the media.

(*a.*) Liquefies gelatine, threads long, interlaced, and unbroken, includes actinomycosis hominis and bovis (Boström and others), and actinmoduræ.

(*b.*) Does not liquefy gelatine, threads broken and often appearing in short forms, actinomyces asteroides (Eppinger), actinomyces Capræ (Silberschmidt).

(2.) Colonies not adherent to media, no offshoots, gelatine not liquefied, threads mostly short with many bacillary forms, examples of the group are actinomyces farcini C, and the organism obtained in Silberschmidt's case 3.

(3.) Growth preferably anaerobic, colonies show no mycelial projections, and on solid media are usually small and sharply circumscribed. No growth on gelatine or at room temperature; the colonies are readily crushed and broken up. The organism does not survive as long as those of groups one and two on artificial media. To this group belong the cultures from six of his human cases as well as those from actinomycosis bovis.

He thinks it too early, however, to attempt a definite division of the pathogenic varieties of the genus actinomyces, and he does not regard pathogenesis as a possible means of diagnosis.

Silberschmidt concludes that:

(1.) Actinomycosis, contrary to the earlier idea, is not a specific infection caused by a single ray fungus, for a number of different micro-organisms may cause the typical disease picture.

(2.) The "drusen," which are not always to be found microscopically, may or may not have peripheral clubs, and are colonies which various micro-organisms may form in tissues.

(3.) The microscopical investigation of the "drusen," or of sections of tissue, permits the finding of the organisms, but not diagnosis of the same.

(4.) Cultures which he obtained without difficulty must be resorted to in order to distinguish the cause of the disease.

(5.) Mixed infection is not the rule in actinomycosis.

(6.) It is not at present possible to distinguish by bacteriological methods between actinomycosis and pseudo-actinomycosis.

(7.) Most of the organisms found in actinomycosis belong to the class of actinomyces, and of this class certain subdivisions are to be made.

Abbott and Gildersleeve [22] have recently pointed out that the various acid-resisting bacilli, distinct from the so-called B. tuberculosis, may form mycelial threads with or without typical actinomycotic peripheral clubs, and may cause larger and smaller inflammatory nodules in the tissues of various animals. As is well known, it has been found by Schulze,[25] Lubarsch,[20] Babes et Levadili,[27] Abbott and Gildersleeve,[22] Friedrich and Nösse,[26] and others that various members of the tubercle bacillus group and other acid-resisting bacilli, as well as streptothrix Eppingeri (Lubarsch), may form branching mycelial threads similar to actinomyces.

Abbott and Gildersleeve urge that these organisms be classed, not as bacilli, but under genus actinomyces.

Lehmann and Neumann, in the last edition of their work, classify as actinomycetes all the delicately threaded organisms free from chlorophyll, with true branching, in part very

abundantly ramifying mycelium, partly with the formation of conidia. This class is further divided into the coryne-bacteria group containing B. diphtheriæ, B. mallei, and B. pseudo-diphtheriæ, B. Xerosis; and Mycobacteria, a group containing B. tuberculosis and the acid-resisting, so-called, bacilli in general; and Actinomyces, a group made up of Actinomyces bovis, Actinomyces farcinicus, Actinomyces asteroides, Actinomyces Maduræ, and the various non-pathogenic actinomyces.

It is certain that our organism belongs to the branch of the actinomyces family in which the formation of branched threads without clubs is more or less constant. Its exact position, on account of its failure to grow on artificial media, must remain unknown. Its marked pathogenicity for rabbits serves to separate it from certain forms most commonly met with in the typical actinomyces of man and cattle.

SUMMARY. Actinomycosis of the central nervous system is rare, we are able to find only five, including our own case, primary and thirteen secondary cases. The disease usually affects males in the prime of life; in the primary cases the age being given as twenty-four, twenty-six, and fifty-two years, respectively, in three cases; not mentioned in two cases. In the secondary group, two were sixteen, five between thirty and forty, one forty-three, and one fifty-two years; age not mentioned in four. Two cases occurred in females. Of the primary, three were reported as instances of "streptothrix" infection and only one (Bollinger) was regarded as typical actinomycosis.

Of the thirteen surely secondary cases, eight were regarded as typical actinomycosis, two as probable actinomycosis, two as cladothrix infection, and one as streptothrix infection.

All of the primary cases except one (Bollinger) were acute, while of the secondary in at least ten the lesions of the nervous system were recent, and usually the cause of death.

The organisms were cultivated in two primary (Almquist and Ferré et Fouquet), and in two secondary cases, in one of which (Eppinger's) aerobic and in the other (Sabrozes et Riviére) anaerobic growths were obtained. Eppinger's

organism was pathogenic for rabbits and guinea-pigs. In
most of the cases neither cultures nor animal experiments
were made, the diagnosis being made from the microscopical
examination alone. No mention is made of any attempts to
test the acid-resisting powers of any of the organisms found.
The so-called actinomycotic granules were recognized in the
pus of several cases. In one, instead of abscesses there were
multiple nodular masses in the brain, and in Bollinger's case
there was a firm mass the size of a hazelnut in the third ven-
tricle and in the foramen of Monro. Primary lesions of the
lungs and bronchial glands were the most common sources
of the metastatic lesions of the central nervous system. In
one case the actinomycotic process extended directly through
the skull to the meninges and brain.

It seems established that, in the present state of our knowl-
edge, all processes caused by micro-organisms having a myce-
lium of branching, interlacing, and sometimes radiating
threads are to be considered as actinomycosis, and that or-
ganisms with the above characteristics, whether or not they
form " drusen " and clubbed hyphæ in the tissues, are to be
regarded as actinomyces.

Further knowledge is necessary before a satisfactory clas-
sification of the actinomyces and the processes caused by
them is possible. To class tuberculosis under actinomycosis
is of doubtful value. It is well to recall, however, that
there are two broad divisions of genus actinomyces as used by
Abbott and others, the acid-resisting (B. tuberculosis and the
acid-resisting, so-called, bacilli) and the non acid-resisting
or acid-bleaching, and that typical tuberculosis is always
caused by the prominent member of the former, and typical
actinomycosis by the prominent member of the latter group.
It is better, with Lehmann and Neumann, to use the term
" actinomycetes " for the large number of organisms of the
latter group. This acid-bleaching group is apparently a
large one, and our knowledge concerning it is best summar-
ized in Silberschmidt's conclusions.

The organism of our case belongs to the branch of this
group in which club formation is inconstant or absent,

pathogenesis for animals is marked, and cultures on artificial media negative.

## BIBLIOGRAPHY.

1. O. Bollinger. Munch. Med. Wochenschr., 1887, No. 41, S. 789.
2. Almquist. Zeitschr. f. Hygiene u. Infectionskrankheiten, 1890, Bd. viii, S. 193.
3. Ferré et Fouquet. Mercredi Medical, 1895, p. 441.
4. Musser, Pierce, and Gwynn. Transactions of Association of American Physicians, 1901.
5. Ponfick. Die Actinomykose des Menschen eine neue Infectionskrankheiten, Berlin, 1882.
6. Köhler. Berlin. Klin. Wochenschr., 1884, Bd. xxi, p. 414.
7. O. Israel. Ibid., 1884, S. 360.
8. Naunym. Mittheilungen aus der Medizinischen Klinik zu Königsberg, 1888.
9. Keller. Brit. Med. Jour., March 29, 1890.
10. Eppinger. Zeigler's Beiträge zur path. Anatomie, etc., 1890, Bd. ix.
11. Sabrazes et Rivière. La Presse Medicale, 1894, Sept. 22, p. 302.
12. Dolore. Gazette hebdomadaire, May 24, 1896.
13. Martin. Journal of Pathology and Bacteriology, 1896, Vol. iii.
14. Chiari. Zeitschr. f. Heilkunde, 1900. Abthiel f. path. Anatomie, i, S. 351.
15. Flexner. Journal of Experimental Medicine, 1898, Vol. iii.
16. Norris and Larkin. Ibid., 1900, Vol. x.
17. Lachner–Sandoval. Inaugural Dissertation, Strassburg, 1898.
18. Hektoen. Philadelphia Monthly Medical Jour.. 1899, p. 615.
19. Kruse. Flügge's Micro-organismen.
20. Lubarsch. Zeitschr. f. Hygiene u. Infectionskrankheiten, 1899, Bd. xxxi, S. 187.
21. MacCallum. Centralblatt f. Bakteriologie, 1902, Bd. xxxi.
22. Abbott and Gildersleeve. Ibid. and Univ. of Penn. Med. Bull., June, 1902.
23. Berestenew. Zeitschr. f. Hygiene u. Infectionskrankheiten. 1898. Bd. xxix, S. 94.
24. Silberschmidt. Ibid., 1901, Bd. xxxvii, S. 345.
25. Schulze. Ibid., 1899, Bd. xxxi, p. 153.
26. Friedrich und Nösse. Zeigler's Beiträge zur path. Anatomie, etc., 1899, Bd. xxvi, S. 470.
27. Babes et Levadili. Arch. de Med. Exp. et d'Anat. Path., 1897, ix, p. 1041.

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# STREPTOCOCCUS MUCOSUS (Nov. Spec.?) PATHOGENIC FOR MAN AND ANIMALS.

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From time to time streptococci have been described which show various points of difference from as well as of resemblance to Streptococcus pyogenes and Streptococcus lanceolatus or Pneumococcus. Among these may be mentioned Diplococcus der Brustseuche der Pferde of Schütz;[1] Streptococcus of contagious pneumonia of cattle of Poels and Nolen;[2] Streptococcus der meningitis cerebro-spinalis epidemica of Bonome;[3] and Streptococcus capsulatus found in spontaneous peribronchitis and multiple pulmonary abscesses in a guinea-pig by Binaghi.[4] We have lately obtained from the peritoneum and various other organs at autopsy on a woman dead of peritonitis a capsulated streptococcus which cannot be classed with either Streptococcus pyogenes or Pneumococcus. The object of this paper is to record our observations on this organism and to compare it with similar streptococci described by others.

*Clinical Summary.* — L. D., female, aged thirty-four years, was admitted to Lakeside Hospital, service of Dr. E. F. Cushing, on May 1, 1900, complaining of pain in the abdomen. Two years before her present illness she had a miscarriage at the seventh month followed by chills and fever. Since this time she had had frequent attacks of pain in the pelvic region. The day before admission she had intense pain in the hypogastrium which was followed by convulsions and coma. Examination of the urine showed albumin and casts.

*Clinical Diagnosis.* — Chronic nephritis, uræmia, chronic pelvic peritonitis.

*Anatomical Diagnosis.* — Chronic tubo-ovarian abscess. Acute fibrino-purulent and chronic peritonitis. Chronic interstitial nephritis with contraction, pyelonephrosis, and pyoureter and chronic cystitis. Œdema and congestion of the lungs and brain. Acute splenic tumor. Enchondroma of the right lung, cyst of the left suprarenal capsule, multiple myofibromata uteri.

The following description of the peritoneum and pelvic organs is taken from the autopsy protocol, the other organs being without present interest:

"The abdomen is somewhat distended; the abdominal and pectoral muscles are fairly well developed. The position of the intestines is normal. The omentum extends to the anterior brim of the pelvis on the right side. On the left side it passes under the coils of the small intestines and is bound by firm adhesions to the structures on the left side of the uterus. The surface of the small intestines, the cæcum, and the descending colon are covered with a thin layer of opaque, grayish-white *viscid* fibrinous exudate. In the dependent parts of the abdomen there is a considerable quantity of creamy pus.

"The contents of the pelvis are matted together, and on the left side are densely adherent to the pelvic brim. The uterus is displaced to the right. The right fallopian tube runs backwards and to the left and, with the ovary, is bound to the uterus. On the left side of the uterus, occupying the position of the left tube and ovary, there is a fluctuating mass the size of a small orange and containing thick pus. Between the bladder and the vagina and communicating with the tubo-ovarian abscess there is an abscess filled with creamy pus containing gas bubbles. The walls of these abscesses are thick and lined with a thick yellowish-gray necrotic material. The left ovary cannot be made out. Besides the large abscess, the tubo-ovarian mass is the seat of a number of smaller abscesses. The uterus is enlarged and in its wall there are several fibroid tumors. The abdominal lymph glands are moderately enlarged."

*Histological Examination of the Tubo-Ovarian Abscess.* —
Sections of the tubo-ovarian mass showed little recognizable
ovarian tissue. The abscess cavity contained necrotic ma-
terial and a large number of polymorphonuclear neutrophilic
leucocytes. Along the borders of the abscess wall there was
a large amount of fibrillated fibrin in the meshes of which
there were variable numbers of polymorphonuclear neutro-
philes. The abscess wall was composed of a granulation
tissue rich in fibroblasts, but rather poor in blood-vessels.
This tissue was infiltrated with large numbers of polymor-
phonuclear eosinophilic leucocytes and with a few plasma cells
and polymorphonuclear neutrophiles. In sections of the wall
of the abscess stained with eosin and methylene blue there were
scattered chains of streptococci and a few short bacilli. The
wall of the left fallopian tube was much thickened and showed
areas of infiltration with lymphocytes, plasma cells, and eosino-
philes. The lumen of the tube contained desquamated epithe-
lium, leucocytes, and necrotic material. The mucosa was
nearly everywhere destroyed and the submucosa was infiltrated
with plasma cells and polymorphonuclear neutrophiles and
eosinophiles. The uterus showed nothing of special interest.
The submucosa of the bladder was infiltrated with large num-
bers of plasma cells. The pelvic lymph glands showed
marked hyperplasia and contained numbers of eosinophiles.

*Bacteriological Examination.* — Coverslip preparations
made from the tubo-ovarian abscess, the kidneys, bladder, and
peritoneum showed large numbers of biscuit-shaped cocci in
pairs, usually arranged in chains of four, six, eight, or twenty
elements, and surrounded by a wide and sharply defined cap-
sule which stained well with Welch's capsule stain. (See
photograph.) In the abscess and bladder there were also
short capsulated bacilli, and in the peritoneal exudate large,
stout capsulated bacilli of the size and appearance of B. aëro-
genes capsulatus. Aërobic Petri-plate agar cultures were
made from the heart's blood, lungs, pleuræ, liver, spleen,
brain, kidneys, tubo-ovarian abscess, and bladder.

The cultures from the brain, pleuræ, left kidney, and liver
remained sterile. In the cultures from the lungs there were

fifteen colonies of Staphylococcus pyogenes aureus and ten colonies of a bacillus which proved on further study to be B. mucosus capsulatus. In the cultures from the peritoneum there were a few colonies of Staphylococcus pyogenes aureus, many of B. mucosus capsulatus, and a number of fine colonies; in those from the tubo-ovarian abscess and bladder there were colonies of B. mucosus capsulatus and a small number of fine colonies. Cultures from the heart's blood gave a few, and those from the spleen a large number of fine pale colonies. Analysis of the above shows that fine pale colonies grew either in pure culture, or mixed with other bacteria (staphylococci and B. mucosus capsulatus) from the heart's blood, spleen, peritoneum, tubo-ovarian abscess, bladder, and right kidney. The fine colonies in all these cultures were similar in every way macroscopically and microscopically.

Secondary cultures from all these cultures were made and studied in various media, and found to be identical. The growth on plain agar, glycerine agar, and glucose agar (neutral to phenolphthalein) was identical, and after twenty-four hours in the incubator at body temperature was made up of a thin, very moist, transparent pale-gray growth. The colonies were small at first, but after forty-eight hours reached the diameter of three millimetres. They were slightly raised, very moist, and had the appearance of dewdrops. Single colonies were round in outline, with regular edges. When magnified fifty times they were of a bluish color and rather coarsely granular, the granules lying in parallel lines. The water of condensation was cloudy and somewhat viscid. There was a growth of fine grayish colonies along the line of the stab. Under the No. 7 lens the young colonies were seen to be composed of long twisted colonies of cocci. No gas was formed.

On alkaline, plain and glucose, agar slants, there was a thin watery transparent grayish growth. Separate colonies showed a concentric appearance. Under the low power the colonies had coarse and fine granulations. There was a thin growth of fine colonies along the line of the stab, without gas forma-

tion. The water of condensation showed a yellowish sedin
ment. After forty-eight hours the colonies were larger and
the growth very transparent and moist.

On blood serum after twenty-four hours in the incubator
there was a thin, moist, pale-gray transparent growth. The
separate colonies were of pin-head size and were round with
regular outlines. When magnified fifty times they were
finely granular.

On gelatine slants (neutral or slightly alkaline) after six
days at room temperature there was a fairly well-marked
pale-gray transparent surface growth. Along the line of
puncture there was a fairly profuse, feathery growth, without
liquefaction.

In neutral and in slightly alkaline bouillon after twenty-
four hours at body temperature no growth was apparent;
after forty-eight hours there was faint cloudiness, with a pale
deposit on the sides of the tube.

On potato (acid reaction) there was no visible growth and
coverslip preparations were negative. Preparations made
from the water below the potato showed streptococci.

Plain and glycerine agar and bouillon $+1.5^5$ showed no
growth; a slight growth was found on glucose agar $+1.5$.

Litmus milk was unchanged after twenty-four hours in the
incubator; on the fourth day there was slight acidity, but no
coagulation. Capsulated biscuit-shaped streptococci in long
chains were present in small numbers.

Optimum growth took place in media made according to
the directions in the " Procedures recommended for the Study
of Bacteria" (American Public Health Association Report,
September, 1897) and rendered neutral to phenolphthalein
and at a temperature of 37° C. It grew fairly well, but
slowly, at room temperature.

The organism grew both aërobically and anaërobically. No
indol was produced in bouillon cultures. It was not motile.

*Morphology.* — The morphology of the organism was very
similar for the various media. It occurred as a coccus, in
chains, the elements of which were arranged in pairs. The
number of cells in each chain varied from two to one hun-

dred or more. The pairs showed marked similarity to the
gonococcus, their elements being biscuit-shaped, separated
by a slight interval, and with the flat surfaces towards one
another. The pairs, including the interval between the in-
dividuals, measured 1.25 to 1.75 m. in length, and 0.5 to 0.75
m. in width. When the excess of light was cut off a definite
halo was seen about each chain. Special capsule stains
failed to stain any definite area, but numerous small, deeply-
stained granules were to be seen within the halo, especially
near its outer borders. The halo varied in width from 1.5 to
3.0 m., and the granulations were not constant. This halo
was more marked about organisms grown on human blood
serum than about those grown on plain glycerine or sugar
agar, gelatine, or bouillon. Cultures in litmus milk showed
the same type, but in this medium the capsules could be
sharply stained by the usual methods. The refusal of the
capsule to stain when the organism was grown on artificial
media was in striking contrast to the action of capsule stains
on the capsules of the streptococci obtained from the tubo-
ovarian abscess, and the peritoneal and other exudates, as
well as from the animal experiments. The streptococci from
both the cultures and from the tissues stained deeply with
Gram's and Weigert's stains, as well as with the ordinary
aniline dyes.

### Animal Experiments.

1. During the autopsy a guinea-pig was inoculated intra-
peritoneally with 0.3 cc. of the peritoneal exudate. The
animal became comatose in thirty-six hours, and died in
forty-eight hours from the time of inoculation.

The autopsy showed no lesion at the point of inoculation,
and no subcutaneous infiltration was to be seen. The peri-
toneal cavity contained between fifteen and twenty cubic
centimetres of a cloudy grayish seropurulent fluid, with
numerous flakes of fibrin. The most notable characteristic
of this fluid was its extreme viscidity, which was such that it
could be drawn out into threads several centimetres long.
The abdominal viscera were heavily coated with grayish

yellow fibrin, which could be readily stripped off, leaving a deeply congested surface beneath. The abdominal and thoracic organs showed no macroscopic changes other than intense congestion. The inguinal and mesenteric glands were distinctly enlarged.

Coverslips and cultures were made from the peritoneal exudate, and from the heart's blood, the liver, and the spleen. Coverslips from the organs were uniformly negative. Coverslips from the peritoneum showed very numerous biscuit-shaped cocci in pairs, usually arranged in chains of four, six, or more elements up to twenty or thirty, and surrounded by a wide and sharply defined capsule. Cultures from the organs were negative, while those from the peritoneal exudate showed a pure growth of a streptococcus. The growth on various media was identical with that from the plates at the autopsy. Forty-eight hours later a series of inoculations was begun to test the virulence of the organism. The series included six guinea-pigs, four rabbits, and one white mouse. The following is an abstract of the results of these experiments:

### Guinea-Pig II.

(*a.*) May 7. One cc. 24-hr. bouillon culture from the growth obtained from guinea-pig I., intra-peritoneal inoculation.

(*b.*) May 12. One cc. 48-hr. glucose bouillon culture of same.

(*c.*) May 18. Two cc. 24-hr. glucose bouillon culture of same.

Died May 28. The autopsy findings were the same as in the case of the first guinea-pig.

Although three successive inoculations were necessary to cause the death of this animal, the virulence of the organism was reëstablished.

Guinea-pigs III., IV., V., and VI. were inoculated intra-peritoneally with fresh peritoneal exudate from previous cases, in decreasing amounts from 1 to 0.25 cc., and died in from twenty-four to seventy-two hours.

Rabbits II. and IV. were each inoculated in the ear vein

with 0.5 cc. of fresh exudate from the peritoneum or subcuta-
neous tissue of guinea-pig and died in twenty-four to forty-
eight hours.

The autopsy findings were similar to those of guinea-pigs
I. and II., except that in all subsequent cases the organism
was recovered in pure culture from the organs as well as from
the exudates. The following are the variations from the
usual type:

In guinea-pig IV. there was a marked exudate into the
pleural cavities, which was of the same type as the peritoneal
exudate.

In guinea-pig V. there was marked thickening and œdema
of the subcutaneous tissues of the abdomen. Bloody fluid,
which contained large numbers of capsulated streptococci, ex-
uded on section.

Rabbit III., inoculated subcutaneously, showed a slight
peritonitis and a marked serous pericarditis, from both of
which pure cultures of the capsulated streptococcus were ob-
tained. The seat of inoculation showed no especial lesion.

In mouse I. none of the serous cavities showed exudate,
and cultures from them were negative, while on the other
hand cultures from the organs showed the wide distribution
of the streptococcus.

Rabbit I. was inoculated in the ear with 0.5 cc. of a
twenty-four-hour glucose bouillon culture from guinea-pig I.
The animal did not die, but extensive local inflammation
and abscess formation took place at the base of the ear. A
portion was excised under ether for microscopical examina-
tion. The ear healed completely after some weeks.

Portions of the various organs of these animals were hard-
ened in Orth's fluid. Sections were stained with hæmatoxy-
lin and eosin, methylene blue and eosin, and Weigert's
fibrin stain. Sections from the hearts, lungs, and kidneys
showed marked congestion. Sections from the livers and
spleens showed marked congestion, but although streptococci
were found scattered through the tissues, no other changes of
importance were noted in the organs themselves. The exter-
nal surfaces of many of the organs were covered with an ex-

udate of varying thickness up to two millimetres. In the cases which died in from twenty-four to forty-eight hours the exudate was composed almost entirely of streptococci with a variable amount of granular and fibrillated fibrin. Most of the few cells which were present were coarsely granular oxyphiles. In the animals living several days, the cellular exudate was much more marked, and in one case was beginning to organize, the process starting from the capsule of the liver. In no case was phagocytosis observed. The organisms did not stain with hæmatoxylin, but were brought out sharply with methylene blue and eosin, and Weigert's fibrin stain.

Guinea-pigs and rabbits inoculated with one and two cubic centimetres of filtered bouillon cultures remained well, showing no signs of illness.

*Summary.* — In this case, therefore, there was a mixed infection with a capsulated streptococcus, B. mucosus capsulatus and B. aërogenes capsulatus. The streptococcus was evidently the most numerous and most important of the organisms present. To it we are inclined to attribute not only the acute lesions, peritonitis, and splenic tumor, but the tubo-ovarian abscess and possibly the chronic nephritis as well.

Schültz's (loc. cit.) coccus was oval, and occurred in pairs and sometimes in chains. It did not stain by Gram's method, and according to Frosch and Kolle[6] should be classified midway between the Pneumococcus and the bacilli of the chicken cholera group. The coccus of Poels and Nolen grew in pairs and chains with a transparent capsule which stained with difficulty. It grew like B. Friedländeri in gelatine (nail-shaped growth) and did not stain by Gram. These two organisms probably belong to the same group, and are possibly identical; the first was pathogenic for horses, rabbits, guinea-pigs, mice, and the second for cows, dogs, rabbits, and guinea-pigs. They are evidently quite different from the organism of our case.

The streptococci of Bonome and Binaghi, however, present a number of points of likeness to our streptococcus and to each other. The streptococcus of Bonome was ob-

tained from the meningeal exudate and lungs of six cases of
epidemic meningitis cerebrospinalis occurring in Padua.
It occurred as an oval coccus, isolated, in pairs, and in
chains. The individual organisms varied in size and were
always extracellular. It was encapsulated in cultures on
certain media and in the exudates of animals, but not in those
of man. It stained with the aniline dyes and by Gram's
method. When grown in bouillon, the medium was rendered
diffusely cloudy with a flocculent sediment, the organisms
growing in long chains without capsules. On agar-agar the
colonies were said to be characteristic, being round and
sharply defined. When magnified fifty or sixty diameters
the deep colonies were oval, markedly granular, of a light
green color, and had sharp borders. The superficial col-
onies were granular in the centre, but showed wavy concen-
tric " layers " at the periphery, having the appearance of
highly refractile filaments. In streak cultures, both on the
surface and in the depth, the growth was in the form of a
semitransparent coating bordering the line of inoculation like
a halo for the distance of 0.5 to 1 mm. or more. In agar-
agar stab cultures, there was a thin dirty gray growth along
the line of the stab, without any surface growth. Coverslip
preparations of this growth showed streptococci surrounded
by a halo, which would not stain by any method tried. The
growth was luxuriant on glycerine agar; the organisms
forming long chains in which the individuals varied in size
and shape, some forms being triangular (biscuit shaped?).
The coccus failed to grow on blood serum, gelatine, and
potato. On artificial media it died out in a few generations
and its virulence was rapidly lost. White mice and rabbits
were quite susceptible and showed fibrinous exudates upon
serous membranes. In mice there was no invasion of the
blood, but in rabbits capsulated streptococci were found in
this fluid. Guinea-pigs and dogs were more resistant, but
were killed and showed local fibrinous and gelatinous exuda-
tions.

Binaghi's capsulated streptococcus, found in spontaneous
peribronchitis and multiple pulmonary abscesses of a guinea-

pig, occurred in pus and pus cells, in pairs and short chains surrounded by a clear capsule which stained deeply (carbol-fuchsin). In bouillon cultures there was considerable growth, made up of streptococci. On agar at a temperature of 37° C. there was a growth of slowly developing dewdrop colonies. There was no growth on gelatine. The organism stained by Gram's method. Two guinea-pigs inoculated with the pus died in four days, and showed at the point of injection a mucoid and hemorrhagic diffuse œdema. The liver, kidneys, and spleen were enlarged. A guinea-pig inoculated with cultures remained alive. It seems probable that the strepto-cocci of Bonome and Binaghi and the organism of our case belong to the same group, and are possibly varieties of Streptococcus lanceolatus. Their points of resemblance are the formation of moist, transparent colonies on solid media, the growth in chains, which are capsulated in certain media and in animals, and their reaction to Gram's stain. They differ, however, in various ways. The colonies vary some-what in shape and appearance. The description of the coccus of Binaghi is too meagre for accurate comparison with the others. The deep agar colonies of Bonome's organ-ism are said to be ball shaped. The peculiar wavy concentric " wrinkling" of the periphery of the superficial colonies of the organism were not present in ours. Unlike the other two streptococci, ours grew well on blood serum and on gelatine. Milk and potato cultures were not made by Bonome and Binaghi; our organism grew in the former, and in the water about the latter. All three organisms are very much alike in their effects upon animals, in which they differ from those of Streptococcus pyogenes; but do not vary markedly from those of Streptococcus lanceolatus. Here, however, they show certain differences, for two of them (Bonome's and our own) produce a hemorrhagic and gelatinous or mucoid œdema in the subcutaneous tissues. We append a table showing the main characteristics of the three organisms. From the foregoing it appears that there is a small group of pathogenic capsulated streptococci, characterized by the viscidity of their growth, and by the formation of gelatinous

exudations in animals. For this group, composed of the streptococci of Bonome, Binaghi, and our case, we propose the name STREPTOCOCCUS MUCOSUS.

## REFERENCES.

1. Ref. in Centralb. f. Bakteriologie, Bd. I., s. 393.
2. Fortschritte d. Med., Bd. 86, s. 217.
3. Ziegler's Beiträge, 1890, Bd. VIII., s. 377.
4. Centralbl. f. Bakteriologie, 1897, Bd. XXII., s. 273.
5. American Public Health Association Committee's Report, 1897.
6. Flügge. Die Microörganismen, 1898, II., s. 161.

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## DESCRIPTION OF PLATE VIIa.

Streptococcus mucosus, from peritoneal exudate, X. 1200.

FIG. 1.

HOWARD AND PERKINS. S. MUCOSUS.

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| De...n. | Potato. |
|---|---|
| Bon... ...aque ut; ... | No growth. |
| Bina...le ...hich ...rep- ...n ...ns. | Not tried. |
| How... Per... 24 n 48 ...t ...s ...le ...h the ...ie | No growth on potato, but some multiplica tion in th water of t bottom of the tube. Milk — in days sligh acidity, n coagula- tion. |

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# Report of Two Cases of Angiosarcoma of the Brain.

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[From the Pathological Laboratory of Lakeside Hospital.]

NEXT to the localization of tumors of the brain and their relation to the tracts of fibers which connect the various parts of the brain with the different organs of the body, perhaps the most interesting study of these lesions is their origin.

The greater part of the cases of brain tumor which are found in the literature are little more than clinical reports of the symptoms and ante-mortem localizations, with a brief statement as to whether the diagnosis was or was not confirmed at operation or autopsy. The pathologic report is ordinarily a mere statement that the tumor was sarcoma, or glioma, or, more frequently, gliosarcoma. This last term, as some of the later writers, notably Taylor (1), have emphasized, is rarely, if ever, an accurate one. The brain is essentially epiblastic in its origin, and if the classification of tumors according to their embryologic sources is to be adhered to, the only tissues in the brain from which sarcoma may arise are the membranes on the outside and the vessels and their sheaths within the brain substance, as these include all the mesoblastic tissues which have to do with the structure of the organ. While the glia tissue subserves the same function to the brain as connective tissue does to the body, it is an integral part of the tissue of the cerebral vesicles, and so must be purely epiblastic. Furthermore it reacts differently from connective tissue, especially chemically, in relation to special stains. It is of course conceivable that a previously formed glioma might be invaded, whether by metastasis, direct invasion, or even possibly by a primary formation about the vessels, by a definite and typical sarcoma. But if such cases have occurred, they have never been reported as such, and it is furthermore probable that the line of demarkation between the two types of new growth could be clearly made out by the microscope.

The following case is of interest as one in which the diagnosis of angio-sarcoma can be definitely made, but in which no trace of special connection with the blood-vessels, either endothelial or perithelial in type, could be made out.

CLINICAL HISTORY--L. R., female, white, 25 years old, married. She was admitted to the Lakeside Hospital, in the service of Dr. Hunter Robb, to whom I am indebted for the clinical report, on February 27, 1899, complaining of persistent vomiting.

The family history was negative, and no record of tuberculosis, tumors, or insanity was obtainable. The patient had always been healthy, with the

exception of the usual diseases of childhood, and she denied venereal disease.

The present illness dated from about four months previous to admission. at which time she began to vomit, usually in the morning. The attacks bore no special relation to the taking of food, but became more and more frequent. until during the three weeks previous to admission she was unable to retain any food long enough to digest it. She had not menstruated since the onset of the vomiting, and believed herself to be pregnant.

On admission, she was in poor physical condition, but beyond the determination of a three to four months' pregnancy, nothing of interest was



CASE I—Angiosarcoma of frontal lobe; ⅓ natural size.

found on examination. The presence of the fetus, associated with the vomiting, led to a diagnosis of vomiting of pregnancy and the patient was treated accordingly. For about a week she was much better, and only vomited once or twice, but on the seventh day after admission, she complained of severe headache and a boring pain in the left eye. External examination of the eyes showed nothing of interest, the pupils were equal, reacted well to light and accommodation, and the symptoms were relieved by the use of blue glasses. During the next week there was marked improvement; the nausea disappeared, and the patient was able to eat the ordinary ward diet without discomfort. On the fourteenth day after admission there was a sudden and

severe attack of vomiting, associated with marked signs of mental aberration. The patient was dull and listless, and on the sixteenth day the knee-jerk could not be obtained. She again complained of pain in the eyes, and an ophthalmoscopic examination was made by Dr. B. L. Millikin, who made a diagnosis of double optic neuritis. On the nineteenth day there was an attempt to induce abortion, in the hope of relieving the symptoms. The patient remained for some days in a partly unconscious condition, with involuntary passage of urine, and occasional twitchings of the arms. During this time the abortion was completed, and the uterus thoroughly cleaned out. There was slight improvement for a day or so, but the patient soon relapsed into a condition of partial, deepening to complete unconsciousness, and died on the thirty-fourth day after admission.

Repeated examinations of the urine and the blood were negative. The temperature, pulse and respiration were about normal until the operation. Following this, they rose steadily until the temperature reached 104°. This was followed by a fall to 101°, coinciding with the temporary improvement. On the thirty-first day it rose to 104°, on the thirty-second to 104.5°, on the thirty-third to 105.8°, and on the thirty-fourth to 106°, taken one hour before death; at this time the pulse was 154, and the respirations 56.

The combination of headache, optic neuritis, and vomiting, together with the fact that abortion failed to relieve the condition of the patient, led to the diagnosis of cerebral tumor. There were no motor disturbances until the very end of the disease, so the probable localization of the growth was thought to be one of the silent areas of the cerebrum. The patient was normally rather dull, but so far as could be ascertained, showed no especial departure from her ordinary psychic condition. This led to a further localization in the frontal lobe, probably the right frontal, as the patient had no affection of the motor speech-center, and was right-handed. The question of operation was discussed, but she was not in a condition to give any hope of a successful result, and died without rallying.

The autopsy was performed sixteen hours after death, the body being still slightly warm.

ANATOMIC DIAGNOSIS — Sarcoma of the right frontal lobe of the brain, without metastases; abortion in the fourth month; fibrinopurulent pleurisy with bronchopneumonia of the left lung; congestion of the liver, spleen, and kidneys; cloudy swelling of the kidneys.

Cultures from the left lung and pleura and from the uterus showed Bacillus mucosus capsulatus in pure culture. Cultures from other organs were negative.

The description of the brain is copied from the autopsy protocol, the other details of which, being without present interest, are omitted.

EXTERNAL EXAMINATION—The skull was symmetric in shape, and of ordinary thickness. The dura was not adherent, either to the bone or to the pia. There was no excess of fluid at the base, and the cranial nerves and other structures at the base appeared normal. The brain was of ordinary size. The blood-vessels of the pia-arachnoid were markedly congested, especially on the right side. The left side of the brain was normal on inspection, but on the right side there was a marked flattening of the convolutions, which were almost obliterated over the anterior portion. On the orbital surface of the frontal lobe, 2 cm. from the inner edge of the hemisphere, and 3 cm. from the anterior tip of the inferior frontal lobe, there was a small dark spot, 1 cm. in diameter, firmer to the touch than the adjacent cortex. The consistency of the entire right cerebral hemisphere was distinctly greater than that of the left, and this condition was especially marked over the frontal and temporal lobes.

SECTION —For various reasons it was necessary to cut up the brain at the time of autopsy. The convexities of the cerebral lobes were removed by a horizontal incision, and vertical sections were then made, about 1 cm. apart.

The medulla, pons, cerebellum, and the left cerebral hemisphere showed nothing abnormal. On the right side, the occipital, parietal and temporal lobes showed nothing but marked congestion of the blood-vessels, both those of the pia-arachnoid and the branches of the cerebral arteries and veins in the brain substance. Section of the frontal lobes showed a tumor-mass involving the anterior portion, and extending back into the region of the Island of Reil. The mass was dark reddish-brown in color, very sharply marked off from the surrounding brain-tissue, and contained numerous vessels in some of which were seen grayish-red adherent plugs. The center was soft and apparently necrotic. In the anterior portion there was a smooth-walled cavity, apparently cystic, containing dark, thick fluid.

The brain was hardened as a whole without further dissection.

Examination of the frontal lobes of the right side, after hardening, showed the localization of the tumor to be as follows:

The mass was roughly oval in shape, its long diameter lying dorso-ventrally. It measured 6 cm. in length by 3.5 cm. in breadth at its widest part.

Ventrally, it extended to a point 1 cm. from the surface of the cortex. dorsally, to a point opposite the lower end of the precentral sulcus, mesially. to within 1 to 2 cm. from the mesial surface of the frontal lobe, and externally to within 1.5 to 2 cm. of the cortical surface. Its lowest point involved the cortex about the dark spot above mentioned, and the upper border reached the plane of the lower end of the fissure of Rolando. With the exception

of the small spot on the orbital surface of the frontal lobe, the tumor lay wholly within the white matter of the hemisphere.

There was everywhere a sharp line of demarkation between the tumor and the surrounding tissues, and over much of the surface the mass could be readily peeled out; there was, however, no definite capsule to be made out. The brain-tissue in the immediate neighborhood showed marked congestion, and seemed to be compressed by, rather than involved in the growth. The structures in the brain were much displaced by the tumor, and in many places the exact relations were difficult to determine. Ventrally, the only gross change apparent was a marked compression both of cortex and of white matter, tending to obliterate the sulci between the convolutions. Dorsally, the mass lay in the neighborhood of the basal nuclei, and thus became relatively more important. The entire *corpus striatum* was lifted up toward the summit of the brain, and displaced backward as well, though it was not in any way involved in the tumor mass, being separated from it by a layer of white matter from .5 to 1 cm. thick.

The right lateral ventricle was much compressed and displaced upward and backward, but had no connection with the cyst-cavity. The general impression given was that the tumor had begun ventrally, where the greater part of the degenerated area was situated, and had grown dorsally, pushing the various structures of the hemisphere before it. The dorsal border approached the motor area, but seemed to have pushed it away, rather than to have involved it, so that the tumor lay wholly within the anterior silent area, Flechsig's "anterior center of association."

The ventral part of the tumor was occupied by a cyst-cavity, containing dark fluid and small pieces of necrotic material. This cyst occupied the upper ventral portion of the tumor, and measured 3 by 3 by 1 cm. in size. It extended ventrally almost to the tip of the tumor, and dorsally about half way to the end.

MICROSCOPIC EXAMINATION -- Pieces were removed from various portions of the tumor and from the cortex for microscopic examination. The methods of examination were as follows:

    1.   Tissues hardened in 4% formaldehyd;
        a.   Hematoxylin and eosin.
        b.   Methylene blue and eosin.
        c.   Van Giesen's picric acid and acid fuchsin.
        d.   Weigert's fibrin stain.
        e.   Weigert's stain for elastic tissue.
        f.   Potassium ferro- and ferricyanid.

   2.  Tissues hardened by special methods for,
      a.  Weigert's myelin-sheath stain.
      b.  Mallory's neuroglia stains.
         1.  Modified Weigert method.
         2.  Phosphotungstic-acid hematoxylin.
         3.  Phosphomolybdic-acid hematoxylin.

GENERAL DESCRIPTION — The brain-tissue in the immediate neighborhood of the tumor showed marked compression, the cells being apparently more numerous than in sections taken from a distance. The blood-vessels were much distended, and many of them contained thrombi, some recent, made up of red blood-corpuscles, leukocytes and fibrin, while others showed beginning organization. There was a uniformly sharp line of demarkation between the tumor and the adjacent brain tissue, and in two places the pia-arachnoid of the inferior frontal sulcus passed down between the two.

The microscopic character of the tumor varied markedly at different points, but its general characteristics were the same throughout. Sections from the various portions showed a very large number of cells, with a scanty stroma, pierced by numerous blood-vessels, both arteries and veins. The cells were large, irregular in shape, with large, round or oval vesicular nuclei, in which numerous karyokinetic figures could be seen. These cells had no particular arrangement, and showed no tendency either to an alveolar structure, or to a perithelial arrangement about the vessels. The stroma was somewhat fibrillar in structure, and contained few cells. The blood-vessels, both arteries and veins, showed many thrombi in all stages, from the most recent to those which had become completely hyaline. Here and there throughout the sections, small emboli broken off from these thrombi were seen, stopping up the course of the smaller arteries. The vessel-walls in many places were increased in thickness, but bore no special relation to the sarcomatous tissue. The central part of the tumor showed complete necrosis, and took no nuclear stains; the inner and deeper portions of the necrotic mass showed no structure whatever, but at the edges the outlines of the cells and the blood-vessels could be readily made out, stained diffusely with the protoplasmic stains. All the blood-vessels in the necrotic area showed thrombi, and the proportion of thrombi in the vessels throughout the tumor was much greater near this area than elsewhere. The necrosis is therefore apparently due to the cutting off of the circulation, causing necrosis *en masse*, or coagulation necrosis.

In the degenerated areas, in some of the thrombi, and also in a few of the cells in the immediate vicinity, there was a varying amount of brownish-yellow pigment, amorphous in type and resembling hematoidin.

In sections from the dorsal portion of the tumor there were numerous giant-cells, with large vesicular nuclei of the same type as those in the prevailing mononuclear cells. Some of these giant-cells contained 8 to 10 nuclei.

In sections from the roof of the cyst it was found that the tumor-cells lay only a few rows deep, immediately adjoining the cyst, and were enclosed by a zone of intense congestion, with thrombi in many of the blood-vessels; beyond this the brain was comparatively normal. Sections from the floor of the cyst, on the other hand, showed this to be composed entirely of tumor.

Pieces were hardened by Mallory's special method for neuroglia, and stained in the various ways recommended by him. Unfortunately the autopsy
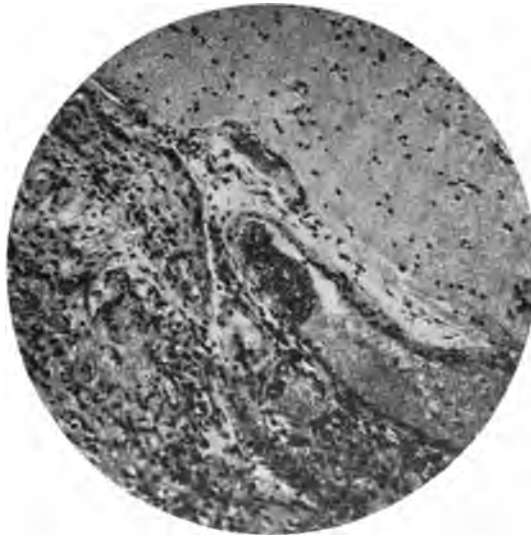


CASE I—Showing line of demarkation between tumor and adjacent tissue—
120 diameters.

was so long after death (16 hours), that the results of these stains, even in the normal cortex, were entirely inconclusive.

Sections of the formalin-hardened brain stained by Van Giesen's method, showed a small amount of rather fibrillar tissue, lying among and between the cells. It took the same stain as the connective tissue of the vessel sheaths, and no connections between cells and fibers could be demonstrated.

Sections stained with Weigert's fibrin-stain showed the presence of large amounts of fibrin in the thrombi in the blood-vessels. The separate fibers were rather thicker than usual, and showed a marked tendency to lie in

bundles, rather than to form a network.  In many places fibrin centers, emanating from leukocytes could be readily made out.  No bacteria of any kind could be found.

Sections from various portions were treated by Weigert's latest method for elastic fibers, in view of the results obtained by Alice Hamilton.[2]  The elastic tissue in the walls of the blood-vessels took the stain sharply, but no bundles of elastic tissue were found elsewhere.

The use of Weigert's method for the staining of medullated fibers failed entirely to demonstrate the presence of nerves in the tumor at any point.

In order to determine whether the pigment which occurred in and about the degenerated areas was a blood-derivative, or melanin, sections were treated for 6 to 8 hours with a 1% solution of potassium ferro-ferricyanid, and placed in acid alcohol for the same time.  The pigment stained diffusely blue, which fact excluded melanin, and therefore melanosarcoma.

In order to determine whether the slight fibrillar network seen with Van Giesen's stain had any connection with the cells, teased specimens were made and stained with phosphotungstic-acid hematoxylin; the cells were found to be of the ordinary polymorphous type, with vesicular nuclei, and in no case were fibers found extending from them.

CONCLUSIONS — In view of the character and arrangement of the tumor-cells, their lack of processes, the minimal amount of stroma, and the sharp line of demarkation between tumor and brain-substance, the weight of evidence seems to be in favor of the diagnosis of sarcoma ; the abundance of vessels throughout the mass, although no distinct relations between them and the tumor could be made out, suggests an angiosarcoma.  On the other hand, the absence of the infiltration of the surrounding tissues, the complete lack of nerve-cells and fibers, and the apparent absence of glia fibers, are against a diagnosis of glioma.

It is true that the failure to stain the glia fibers in portions of the brain where they are known to exist, prevents an absolutely final conclusion, but a view of all the points noted leads to the belief that the tumor is an angiosarcoma, and bears no special relation to the neuroglia tissue of the brain.

In connection with the case reported above it is of interest to consider another case of intracranial tumor somewhat similar to it in which the microscope places the diagnosis beyond doubt.  The specimen was found in the pathologic museum of the Western Reserve Medical College where it had been placed a number of years ago by the late Dr. I. N. Himes.  The history accompanying the specimen states that it was obtained from a woman 45 years old who had paralysis and spasmodic muscular twitchings of the left arm.

At autopsy a tumor was found lying under the center of the left cerebral hemisphere, about the shape of a flattened orange and measuring 9x6x5 cm. in its various diameters. The surface was irregularly lobulated, being apparently constricted by narrow fibrous bands. The consistency was firm, and the whole mass could be readily shelled out from the surrounding brain-tissue. There is no record of the exact relations, and the specimen preserved consists only of the tumor and a thin slice of brain-tissue overlying it.

The hardened specimen was dense in consistency, and cut somewhat like fibrous tissue. It was surrounded by a definite fibrous capsule. The specimen was hardened and preserved in alcohol. Pieces were removed from various portions of the tumor and brain-tissue and imbedded in celloidin. Sections were stained with hematoxylin and eosin, methylene blue and eosin, and Van Giesen's picric-acid fuchsin.

MICROSCOPIC EXAMINATION — Sections from the surface of the tumor mass show a fibrous capsule of varying thickness, usually about 1 mm. from which fibrous bands run down into the tissue at points and lines corresponding to the depressions and lobulations noted in the gross description.

The growth is very cellular, and the most striking point about its appearance under the low power is the arangement of the cells. These lie in numerous concentric whorls of various size, some almost circular, others oval, while still others are much elongated and elliptical in shape. Closer study with higher powers shows that a very large number of these whorls bear definite relations to blood-vessels of varying size which constitute the centers about which the cells are arranged. The angles at which the vessels are cut modify the shapes of the whorls, as the cells lie parallel to the lumina of the vessels. In some of these vessels the lumina persist, in others they are filled with cells lying in concentric layers; in others they are filled with hyalin material often arranged in concentric layers and staining a deep pink with Van Giesen's stain. In some of these concentric hyalin masses a few cell-outlines can still be traced. In many cases in sections stained with hematoxylon and eosin, or with methylene blue and eosin, no vascular center can be definitely made out even with the oil immersion, but in many of these areas the use of Van Giesen's stain shows some remnant of tissue staining pink, usually with no special form. It seems at least probable that these are remnants of the original central blood-vessel whose walls have been infiltrated and compressed by the tumor-growth until there is only this trace left behind to show the origin. In other words such places seem to be an intervening stage between the whorls with a definite vascular center and those in which no trace of vessel persists. The cell proliferation can be traced directly from the adventitia into the tumor-mass, though it is interesting to note that the

hyperplastic tissue at once ceases to take up selective connective-tissue stains such as Van Giesen's. The cells composing the tumor are mainly of one type or are slight variants from it. They are large, oval, or spindle-shaped with large oval vesicular nuclei, and lie in a minimal amount of stroma. Some of the cells, especially those in the immediate vicinity of the vessels, are much elongated and flattened, while the cells which lie at the meeting-point of several whorls are often almost round. Here and there are scattered a few cells of another type, smaller, round or oval, with nuclei containing much more chromatin than the other cells, but with no demonstrable processes. There is nowhere any inflammatory reaction, nor any cell-infiltration, nor is there any excess of leukocytes in the vessels. No thrombi are seen in any part.

The growth appears to have been slow, as there are very few nuclear figures to be seen. No nervous-tissue elements, whether ganglion-cells, glia-cells and fibers, or medullated fibers, could be demonstrated. The encapsulation and sharp differentiation from the brain-tissue, the vascularity, the abundance of cells with minimal stroma between them, and the absence of nervous elements, point to the diagnosis of angiosarcoma, while the definite arrangement of the cells about the blood-vessels, and their evident origin from the adventitia, place the tumor under the head of the perithelial angio-sarcomata. Inasmuch as a very small amount of brain-tissue in addition to the tumor was preserved, it was not possible to follow out the lesions causing the clinical symptoms.

The nomenclature of tumors of the brain has been the subject of much discussion for a long time. Until the embryology of the cerebral vesicles was carefully worked out there was no definite basis on which to go, and solid tumors of the brain-substance as well as those of the membranes were put together under the head of sarcomata. Even since the cerebral vesicles have been finally classed as entirely epiblastic in origin, there is much diversity in definition even among the best authorities. A sharp differentiation between the terms sarcoma and glioma is rarely made, and the combined name gliosarcoma is still in common use.

A brief summary of views of some of the more important writers will show this clearly. Orth[3] states that if fibers predominate we have a pure glioma, but if there are many free cells we can diagnose gliosarcoma. Thoma lays stress in his text-book on the epiblastic origin of glioma, but admits the possibility of gliomata undergoing a change and passing over into rapidly growing gliosarcomata. Birch-Hirschfeld also allows the term gliosar-coma, and makes as his only distinction between glioma and sarcoma the richer development of cellular elements and the greater size in the latter.

Oppenheim[6] admits the possibility of mixed tumors, and Starr[7] uses the term gliosarcoma in his text-book. Virchow[8] bases the diagnosis on the character of the cells. In a glioma the cells have processes, nerve-cells and fibers are absent, the cells are few and the ground-substance is permanent. In sarcoma on the other hand there are numerous polymorphous cells without processes, and the cement substance is scanty. Ziegler[9] states in the last edition of his text-book that true gliosarcoma may occur when a perivascular, adventitial cell-growth whose product forms an integral part of the tumor enters a



CASE II—Showing concentric arrangement of cells—800 diameters.

glioma. Strœbe[10] agrees with Ziegler. Thomas and Hamilton are of the opinion that all new growths of the brain are to be regarded as gliomata unless they can be proved to conform the vessel-walls. They use the term gliosarcoma however in describing a rather cellular tumor in which the cells possess definite processes. Taylor in his extensive article on neuroglia in connection with which he reports two cases distinguishes between gliomata in which the fibers are still undifferentiated and older forms in which they are more or less completely so. In view of the embryonic origin of the tissues involved, he excludes gliosarcoma as a definite tumor, although he also states that there is as yet no fundamental distinction between glioma and sarcoma. Von Lenhossek[11] states that a sarcoma cannot be a glioma.

### LITERATURE.

1. Taylor—*Journal of Experimental Medicine*, 1899.
2. Thomas & Hamilton—*Journal of Experimental Medicine*, 1899.
3. Orth—*Pathologie und anatomische Diagnostic.* Berlin, 1894.
4. Thoma—*Lehrbuch d. pathologischen Anatomie*, 1894.
5. Birch-Hirschfeld—*Lehrbuch d. pathologischen Anatomie*, Bd. II, S. 382.
6. Oppenheim—*Die Geschwuelste des Gehirns.*
           *Spezielle Pathologie u. Therapie*—Nothnagel, Bd. IX, S. 1.
7. Starr—*Brain Surgery*, New York.
8. Virchow—*Die krankhaften Geschwuelste.*
9. Ziegler—*Lehrbuch d. pathologischen Anatomie*, Bd. II, S. 363.
10. Stroebe—*Ueber Entstehung von Band Gehirnglioma.*
           *Ziegler's Beitraege z. path. Anat. u. allg. Path.*, 1895, S. 405.
11. Von Lenhossek—*Die feinere Hau des Nervensystems.* Berlin, 1895.

To HUNTER ROBB, M.D.

*Visiting Gynecologist to the Lakeside Hospital, Cleveland, O.:*

I have the honor to submit the following brief résumé of the work done in the Gynecological Department of the Pathological Laboratory of Lakeside Hospital during my term as Resident Gynecologist from January 1, 1898, to January 1, 1901. My hearty thanks are due the assistants connected with the Gynecological Service for their valuable aid in carrying out this work, and also to Dr. W. T. Howard, Jr., the Director of the Pathological Department of the Hospital, for kindly advice.

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WILLIAM H. WEIR, M.D.,

*Resident Gynecologist, Lakeside Hospital.*

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# A REPORT IN GYNECOLOGICAL PATHOLOGY.[1]

BY

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of Gynecology, Western Reserve University,
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THE routine pathological examination of all tissues removed
at operation has been carried out in the gynecological depart-
ment since the opening of the new hospital building in January,
1898. From this date to January 1, 1901, 523 operative cases
supplied tissues for examination, a brief résumé of the findings
being given in this paper. Of course operations such as ventral
suspensions of the uterus in which no tissues were removed, or
vaginal punctures with the evacuation of pelvic abscesses in
which merely cultures were made, are not included in these 523
cases. Although frequently the microscopic findings in a single
instance may seem of little interest, the study of any extensive
series of similar cases cannot fail to render the observer familiar
with the various stages of similar pathological processes and thus
lead him to a correct interpretation of the appearances in a given
case, which might still remain obscure to one not familiar with
the possible changes in these tissues. Valuable statistics may
also result from this routine work when it has been carried out
for a sufficient time, and occasionally special interest will be
aroused by finding a totally unsuspected pathological condition.
Moreover, the microscope sometimes affords us the means of
making an early diagnosis, so that operative measures can be
instituted at a period when complete removal of the disease can
still be hoped for.

*Examination of Tissues.*—The tissues were fixed as soon as pos-
sible after operation. Curettings were hardened usually in
alcohol, but formalin has been employed lately with good results.
Larger specimens, such as ovaries, were sketched and the gross
appearances described, the weight and measurements being also
given. Cover-slips and cultures of pus, if present, were made
and fluids from cysts examined. As a rule these specimens were

[1]From the service of Dr. Hunter Robb and the Pathological Labora-
tory of the Lakeside Hospital, Cleveland, O.

hardened in Orth's (formalin-Müller) fluid, embedded in celloidin, and stained with hematoxylin and eosin. The sections having been examined, the description of the microscopic appearances was also added; the loose sheets, upon which the records were made, were subsequently bound, and a comprehensive card index was made. From time to time the slides and records were inspected and the diagnoses corroborated by the visiting pathologist, Dr. W. T. Howard, Jr.

The resident gynecologist upon this service, besides assisting the visiting gynecologist, Dr. Hunter Robb, in all operations, had direct charge of the pathological work of the department. This was frequently a great advantage, especially in very adherent cases in which the specimens removed were much distorted, as the relations and conditions at the time of operation were known, and as a result the pathological investigation was much facilitated.

Besides the routine technique above described, special methods of fixing, embedding, staining, etc., were constantly being carried out, and, thanks to the courtesies extended to us by our colleagues, interesting gynecological cases occurring in the other services of the hospital were frequently examined also in our department, although these do not appear in our figures.

### CLASSIFICATION OF MATERIAL.

I. UTERINE LESIONS. *Endometritis.*—In the diagnosis of the inflammatory conditions of the endometrium writers vary widely. In such a tissue, presenting at different epochs so many appearances, all of which may be normal, the personal equation necessarily plays a prominent part in making a diagnosis, more especially as different hardening agents will make a decided difference in the appearance of the tissues. In the classification adopted three main groups were made: (1) glandular hypertrophy, (2) glandular hyperplasia, (3) interstitial endometritis, although it is hardly necessary to state that combinations are the rule. In the presence of the first two no actual inflammatory change may be demonstrable, although these conditions are usually included under the general head of endometritis. By *glandular hypertrophy* is meant an increase in the size of the glands, due to an increase of the glandular elements—the epithelium—so that, although the actual number of the glands remains the same, the multiplication of the epithelium which preserves its single layer produces elongation and dilatation of the gland with the result-

ing twisting, pouching, convolution, or invagination so frequent-
ly seen.  Many of the hypertrophic cases may strongly suggest
*hyperplasia,* by which is meant an increase in the number of the
glands, although the size may remain normal; but the majority
are instances of true hypertrophy, and the hyperplastic appear-
ance is to be explained by the occurrence in a number of sec-
tions of different portions of the same convoluted gland.  The
two conditions of hypertrophy and hyperplasia may exist to-
gether, but a purely hyperplastic condition is but seldom seen.
The interstitial form, as the name implies, affects the stroma,
the glands being only secondarily affected—for instance, by an
atrophy resulting from the contraction of the connective tissue.
Both acute and chronic forms are seen, the former characterized
by a marked cellular infiltration, the latter by a fibrosis.  It
is with respect to this chronic type that such a difference of
opinion exists, many writers believing the condition to be prac-
tically normal, except in very marked cases, while others regard
it as pathological.  Our classification has been made in accord-
ance with the latter view.  The following is a table of our find-
ings:

NUMBER OF CASES OF ENDOMETRITIS EXAMINED.

Glandular  hypertrophy.................................. 62
Glandular hyperplasia...................................  3
Endometritis interstitialis acute.........................124
     "            "            chronic  .....................  21
Glandular hypertrophy  with hyperplasia................ 10
     "         "         "          "        and acute inter-
     stitial  endometritis................................  1
Glandular hypertrophy with hyperplasia and chronic inter-
     stitial  endometritis................................  5
Glandular hypertrophy with acute interstitial endometritis.  8
     "           "          "   chronic    "            "      38
     "        hyperplasia    "       "         "           "        1

Decidual tissue and placental remnants associated with marked
cellular infiltration occurred in 47 cases (not included above) of
curetting after abortion.

*Tubercular endometritis* was found once, Path. No. 312.  The
true condition was unsuspected before operation, but the micro-
scopic appearances were unmistakable.  In a case of tubercular
pyosalpinx the endometrium, although showing a very marked
acute interstitial endometritis, failed to present recognizable
tubercular structure.  *Polypoid endometritis* was well marked in
4 cases, 2 being associated with fibromyomata of the uterus.

Malignant *adenoma* of the body of the uterus, differentiated by Gebhard from the ordinary adenocarcinoma of the uterus by the fact that the epithelium retains its single layer, occurred in one case. A curetting was first performed for diagnosis and the uterus subsequently removed by vaginal hysterectomy. Several small areas of the diseased condition were found upon the left lateral and posterior surface of the endometrium; the process was at an early stage, the muscularis not being appreciably implicated. The appearance was very characteristic, the stroma being reduced to a minimum; the epithelium was pale and swollen, and showed numerous karyokinetic figures.

*Sarcoma* of the uterus occurred in three cases. These have been reported more fully elsewhere.[1] The first case was one of myofibroma sarcomatodes uteri arising from a myofibroma of the uterus; development of the tumor was traced from both unstriped muscle and connective-tissue cells; the uterus weighed 3,750 grammes and measured 20 x 18 x 18 centimetres. Another case was one of myosarcoma uteri developing from a fibromyoma of the uterus through sarcomatous transformation of the connective-tissue elements. In the same uterus were found multiple fibromyomata showing calcification and hyaline degeneration. The uterus in this case weighed 4,700 grammes and measured 28 x 19 x 15.5 centimetres. The third case proved to be an instance of smooth-muscle-celled sarcoma, due to the transformation of muscle and connective-tissue cells of the uterine wall without the previous existence of a fibromyoma. The uterus was not so large as in the other cases, weighing but 450 grammes, but the growth was exceedingly malignant and active. The patient died eighty days after operation, numerous metastatic growths in the lungs and a local recurrence being found at autopsy.

*Fibromyomata* uteri occurred in 24 cases. In 11 of these the tumors were small and removed by myomectomy, 5 being the maximum number in a single case, the heaviest of these small tumors weighing 39 grammes. In the remaining 13 cases, myomectomy was twice performed, and supravaginal hysterectomy in the others. Path. No. 226 was a submucous fibroid weighing 565 grammes and measuring 14 x 10 x 7 centimetres. It was removed per vaginam after the narrow pedicle attaching it to the fundus uteri had been severed with an écraseur. The specimen was exhibited by Dr. Robb before the Cleveland Medical Society

[1] Weir, W. H.: Muscle-Cell Sarcomata of the Uterus. AMERICAN JOURNAL OF OBSTETRICS, May, 1901.

November 24, 1899. Path. No. 256 presented a fibromyoma weighing 1,780 grammes and was associated with a fibroid of the ovary. This case was reported more in detail by the writer in THE AMERICAN JOURNAL OF OBSTETRICS, vol. xlii., No. 3, 1900. Path. Nos. 374 and 467 showed a combination of myoma and sarcoma and have been mentioned above. The largest myomatous tumor removed weighed 4,055 grammes. Hyaline and fatty change and calcification were found in different specimens, and the presence of mast cells in sections stained with carbolic toluidin blue was frequently noted. Although in many of the cases the tumors were very adherent and difficult to remove, recovery occurred in every instance.

*Metritis* was well marked in 7 cases. Path. No. 131 was from a hysterectomy in a case of complete prolapse of the uterus complicated with pregnancy which had terminated by abortion at the third month. Path. No. 295 was a case of suppurative metritis due to streptococcus infection following an abortion from a uterus septus partialis. The uterine wall was riddled with abscess cavities, and a tubo-ovarian abscess upon the left side seemed to have been due to infection through the uterine wall, since the lumen of the tube, except at the extreme outer end, presented a perfectly normal appearance. Most of the remaining cases of metritis were found in connection with fibromyomata for which hysterectomy was performed. The small number of these cases of metritis is accounted for by the fact that this diagnosis was not counted in cases which were simply curetted, and that wherever possible conservative operative measures were adopted and the uterus was not removed.

*Subinvolution* was the diagnosis in one case. The uterus was much enlarged, the wall being from 3 to 5 centimetres in thickness and showing great numbers of mast cells. No actual inflammatory cellular infiltration was found. This patient had grown tired of conservative treatment and insisted upon a hysterectomy.

A normal uterine wall occurred a number of times in cases of fibromyoma, the sections being taken from unaffected areas.

*Cervix.*—Fibroadenomatous polypi were removed in 5 cases.

*Carcinoma.*—Thirteen cases furnished material for examination; all of these when admitted were in an advanced condition, hysterectomy being performed but once. This case was a *nullipara* who subsequently died from a recurrence. The case is reported more in detail by the writer in THE AMERICAN JOURNAL OF OBSTETRICS, vol. xlii., No. 3, 1900.

In the remaining cases curetting and cauterization was performed, sometimes being repeated; in all the disease was advanced and palliative measures alone were considered advisable. All the carcinomata of the cervix were of the epithelioma type except Path. Nos. 44 and 83 (two specimens of tissue from the same case at different times); the growth in this instance was apparently adenomatous. The occurrence of marked cellular infiltration with eosinophilic leucocytes was noted very frequently in these cases.

The following diagnoses were also made: *Cervicitis,* 18; *erosion* (true), 2; *adenomatous formation,* 8; *hypertrophy,* 3.

*Scar tissue,* formed after trachelorrhaphy, was removed in one case where there was suspicion of beginning carcinoma, but this was not confirmed on microscopic examination.

II. OVARIAN LESIONS.—Fibromata were found in two cases. Path. No. 91 was a small pedunculated growth from the ovary; the sulci upon the surface showed germinal epithelium; perioöphoritic adhesions were present and a catarrhal salpingitis.

Path. No. 256 was a case of fibroid of the ovary associated with fibromyomata of the uterus and has already been referred to under the latter heading. The ovarian tumor, measuring 9 x 8 x 6.5 centimetres, was of stony hardness and consisted of dense interlacing fibrous tissue with very few recognizable ovarian structures.

A single *dermoid cyst* (Path. No. 38) was met with. The cyst, measuring 24 centimetres and 26 centimetres in circumference, was non-adherent and the tube was normal. The contents consisted of sebaceous matter, which solidified after the cyst was removed, a sweat-like fluid, and a quantity of hair. The wall showed skin, cartilage, bone, several teeth, striped muscle, and lymphadenoid tissue. Upon one side of the tumor were found the remains of the ovary, which presented a normal appearance.

Multilocular *adenocystoma* was found but once and at a very early stage. The main cyst, being only 1 centimetre in diameter, was thought to be a Graafian follicle until examined microscopically, when its appearance was found to be most characteristic. Unsuccessful attempts were made to trace its origin, but the Wolffian ducts in the mesosalpinx, although in close relation, showed no connection with the cyst and the epithelium was of an entirely different type. No connection with the germinal epithelium upon the surface could be found. The cyst epithelium was tall and narrow and showed numerous goblet cells. The

whole ovary weighed 12 grammes and contained a number of Graafian follicles of normal appearance.

Multilocular papillary *adenocystoma* occurred twice. Path. No. 164, a large cyst upon the left side with a number of smaller cavities contained 1,620 cubic centimetres of fluid which coagulated with heat and showed a specific gravity of 1.042. The contents of the different cysts varied in color considerably. The right ovary was not so enlarged, but showed a papillomatous growth both upon the surface and also in the interior. In character it was rather solid than cystic, but microscopically both sides were found to consist of arborescent papillary growths covered with a single layer of regular columnar epithelium showing cilia. Psammomata were very numerous. Path. No. 237 showed upon the right side a large multilocular cyst weighing 1,450 grammes; the pedicle was firmly twisted a number of times and the vessels in it were thrombosed. The cyst was adherent upon all sides to the intestines, and the only parts of the tumor which took the stain were in the immediate vicinity of these adhesions. The great bulk of the tissue showed no nuclear staining, although the papillary structure was plainly visible. Both the tissue and the cyst fluid were hemorrhagic. The left cyst weighed 1,105 grammes and was also multilocular. The tissue stained well and showed a well-marked papillary structure covered by a single layer of columnar epithelium. Psammomata were found in small numbers. No microscopic evidence of carcinomatous change was found in either of these cases, and clinically they would appear benign, since, although the condition was far advanced, at the present time, more than two years after the operations, the patients are alive and well and show no evidence of recurrence.

Multilocular papillary *adeno-cysto-carcinoma* occurred twice. Path. No. 28 was an advanced case and proved to be inoperable. When an exploratory incision was made the ascitic fluid and a small nodule for pathological examination were alone removed. Shortly afterward the patient died, and a subsequent autopsy revealed a very extensive implication, the uterine wall, bladder, and rectum being invaded, and diffuse implantations being found throughout the abdomen. Microscopically the papillary growth was very luxuriant, completely filling most of the cyst cavities. The epithelium showed active proliferation and was stratified, irregular in shape, swollen, and with dark nuclei frequently showing karyokineses. No psammomata were found.

Path. No. 160 was also an advanced case in a woman aged 67. The cyst was multilocular and 16 centimetres in diameter. The papillary processes extending into the cyst cavities were covered, as a rule, with stratified epithelium as in the preceding case, but in some areas the appearance resembled that of a simple papillary cyst, the epithelium being regular, columnar, and in a single layer. Large areas of the tumor were degenerated and did not stain; no psammomata were found. This patient died some three months after operation, numerous metastases being found at autopsy.

In both of these cases the appearance was typically carcinomatous, and it is of interest to note that no psammomata were found in them, while these bodies occurred in the two simple papillary cysts mentioned above. This, however, is by no means always the case, since they are usually found in the malignant cases as well.

*Papilloma* of the ovary was found twice. This condition really corresponds with the papillary adenocystoma, and one of the instances occurred in Case No. 164, mentioned under the latter heading.

Path. No. 439 showed a small superficial papilloma of the ovary covered in by adhesions which bound the tube and ovary together. The papillæ were not complex; the epithelium was regular columnar and in a single layer; psammoma bodies were also noted. In this case the point of origin seemed to be in the germinal epithelium upon the surface of the ovary.

*Corpus-luteum cysts* were frequently found, but were usually of small size. In many instances it was impossible to distinguish between these cysts and Graafian follicles which had lost the membrana granulosa and into the cavities of which hemorrhage had occurred. Eosinophiles were noted quite often in the walls of the cysts of the corpus luteum.

*Follicular hypertrophy (hydrops folliculorum).*—A number of cases occurred in which a single Graafian follicle had become much enlarged, 5 or 6 centimetres in diameter, the ovarian tissue being stretched out so as to form a thin investing shell. Microscopically many of these showed an apparently normal lining of membrana granulosa; in others this was missing, and in still others hemorrhage had taken place into the cysts. This diagnosis was also made in a few cases where the ovary was considerably enlarged and filled with a large number of Graafian follicles up to 1 centimetre in diameter. Ovaries showing this latter condition alone were rarely removed at operation in our service.

*Ovarian abscess* was found in 30 ovaries; in some cases the condition was bilateral and it was usually associated with pyosalpinx.   Streptococcus pyogenes was found in two cases; in most of the others there was a gonorrheal history, and although the gonococci could not be found in the abscess, they were occasionally demonstrable in the tubes in the same cases.   In almost every case of ovarian abscess there was very marked cellular infiltration with eosinophiles.[1]

*Oöphoritis.*—Inflammatory cellular infiltration of any considerable extent was seldom found, except in association with ovarian abscess, only 12 instances being noted, although in cases of perioöphoritis the process might be very active and intense. The inflammatory infiltration was usually sharply defined by the tunica albuginea and rarely had invaded the ovarian tissue proper.   The small-celled infiltration found in advanced corpora lutea and around small corpus-luteum cysts was hardly considered as pathological.

*Perioöphoritis* was the most frequent condition found in the ovary.   It was usually limited to the outer surface and rarely invaded the ovary itself.   As an acute condition it occurred in 9 ovaries, not including cases of ovarian abscess, while a more chronic form occurred in 119 ovaries.   In these latter fibrous adhesions were found binding the ovary to the surrounding structures; beneath the adhesions were frequently seen inclusions of germinal epithelium and peritoneal cells which presented a most varied appearance as to type of cell and arrangement.   A series of changes was noted quite frequently by which there resulted from these epithelial inclusions well-marked calcified concentric bodies, identical with the psammomata found in papillomatous cysts of the ovary.   These bodies were found 31 times, in 7 instances the condition being bilateral.   No doubt they occur far more frequently than these figures would suggest, since in a single ovary they are not very numerous and are apt to be torn out of the section during cutting.   The psammomata, as a rule, occur near the surface, but in a few instances they were found deep down in the ovary in connection with tubular epithelial structures.   Path. No. 466 showed this condition well; the tubes and ovaries on both sides were adherent; there was a small hydrosalpinx upon the right side and a pyosalpinx upon the left.

[1]Weir: Eosinophiles, etc. (to appear shortly).

Throughout all parts of the ovaries were found narrow tubules which occasionally branched; they were lined with a single layer of deeply staining irregular columnar cells; they closely resembled the Wolffian ducts in the mesosalpinx, and also seemed similar to down-growths from the germinal epithelium. The condition was neither cystic nor papillary, and there was no suggestion of malignancy. In a few places psammoma formation was noticed in relation to the tubules; a somewhat similar appearance, but limited to the outer part of the ovary, was found in 3 other cases, in which they were apparently formed by down-growths from the germinal epithelium.

*Parovarian cysts* occurred in three cases. Path. No. 457 showed a small cyst containing about 3 ounces of fluid with a large amount of cholesterin. The epithelium was flattened and in a single layer.

Path. No. 461. The cyst measured 10 x 10 x 7 centimetres in three diameters and weighed 270 grammes. It presented a typical appearance, the tube being stretched out over the cyst and the ovary being normal. The epithelial lining in a single layer was columnar or cuboidal and non-ciliated.

Path. No. 487. This cyst was torn to pieces during removal, owing to the numerous adhesions. The epithelium was flattened and in a single layer.

Numerous instances of parovarian cysts of small sizes were met with; some of these it was very difficult, or even impossible, to differentiate from peritoneal formations due to inclusion of cells beneath adhesions.

*Senile ovary* was the diagnosis in 34 instances and *normal ovary* in 21. In these there was no appreciable pathological lesion; many were removed with uterine fibromyomata, others in tubal disease such as ectopic gestation, or more rarely for symptomatic reasons.

III. TUBAL LESIONS.—Tubo-ovarian cysts occurred in two instances. Path. No. 178 showed a tumor weighing 885 grammes and measuring in circumference in two diameters 37 centimetres and 32 centimetres. The tube was greatly distended, and in the cavity formed by the tube and ovary were 775 cubic centimetres of dark fluid. The epithelium in the tube was lower than usual and in the ovarian portion of the cyst consisted of a single layer of cuboidal or flattened cells. In this situation were found several flattened plaques, 1 to 1.5 centimetres in diameter, slightly elevated from the surface and black in color. On microscopic-

examination these seemed due to subepithelial hemorrhages which had become organized.

Path. No. 219.   This cyst was ruptured during removal, owing to the numerous adhesions.   It was smaller than the other case, but the character of the epithelium was the same.

*Hydrosalpinx* was found in 23 tubes.   In some cases the condition was bilateral; in one case there was torsion at the cornual end with resulting infarction.   The ovary was not involved in the constriction.   This accident in the tube alone is of rare occurrence, and this case is more fully reported elsewhere.[1]

*Hematosalpinx.*—Three cases are recorded.   In one there was a ruptured ectopic gestation in the other tube, which probably accounted for the blood in the hematosalpinx, the closure of the fimbriated extremity having probably resulted from the subsequent inflammatory action.   Another case occurred in connection with a myoma of the uterus; the infarcted hydrosalpinx just mentioned was practically a hematosalpinx, but is not included in the above three cases.

*Tubal pregnancy.*—Five cases were met with.   Path. No. 221 was operated upon per vaginam.   The condition was very chronic and unsuspected.   The chorionic villi were much degenerated and difficult to recognize.   The other tube showed a pyosalpinx containing B. mucosus capsulatus.   In two of the cases rupture had occurred through the dorsal surface about midway between the cornu and the fimbriated extremity, but, although the clots were carefully examined, no fetus could be found.   In another case there had been a tubal abortion with the formation of a large hematoma at the fimbriated extremity, limited in extent by the formation of adhesions.   The rupture had occurred some time before operation, and the true condition was unsuspected.   Upon careful inquiry there proved to have been no suggestive symptoms.

*Sarcoma* of the tube was found as a metastasis in the mucosa occurring in a case of uterine sarcoma previously mentioned.

*Tuberculosis* occurred in three instances.   Path. No. 266 showed a right pyosalpinx and a left salpingitis, the condition answering to the so-called salpingitis isthmica nodosa.   The epithelial tubercles were well marked, but no giant-cell formation was noted.   The endometrium showed a very intense inter-

[1]Weir: Torsion of a Hydrosalpinx Resulting in Infarction. AMERICAN JOURNAL OF OBSTETRICS, vol. xlvi., No. 4, 1901.

-stitial endometritis, but without recognizable tubercular lesions. The other two cases were very chronic.

Path. No. 144.  Both tubes were removed for chronic salpingitis and a small myoma was excised by myomectomy.  The left tube showed a slight grade of chronic tuberculosis unrecognizable from the gross appearances.  Tubercular lesions could not be found in the other tube.

Path. No. 308 showed at operation recent small tubercles over the intestines.  In both tubes there was a slight but very chronic tuberculosis with calcification.  The ovaries failed to show tubercular lesions.  Unless our attention had been directed to the cause by the peritoneal lesions, the true condition might readily have been overlooked.

*Pyosalpinx* was found in 65 cases, most of these being bilateral. There were seven other tubes, not included here, removed for presumptive acute salpingitis in which there was a small amount of purulent exudate between the folds—more properly, a catarrhal salpingitis.  The infective agent in 7 cases proved to be gonococcus from cover-slip examination and stained sections of the tissues.  The history in a great many other cases was suggestive, but not proved by the finding of the organisms.  Streptococcus pyogenes occurred twice; B. mucosus capsulatus and staphylococcus pyogenes albus and B. tuberculosis once each.  In the histological examination of these cases we were struck by the almost invariable presence of eosinophilic cells in the cellular infiltration.  A special article dealing with this has been referred to under the head of ovarian abscess.

Another point of interest is the remarkable persistence of the epithelium upon the folds of the mucosa in pyosalpinx.  The cells may be so swollen and pale, and the intercellular spaces so filled with inflammatory cells, that the epithelium is scarcely distinguishable from the swollen connective-tissue cells of the folds. A certain amount is, of course, lost, as is shown by the numerous adhesions forming between the folds; but a large part remains, and in the least affected areas the cilia are often retained.  In the advanced cases the outline of the mucosa becomes much distorted, and consequently epithelial diverticula from the mucosa are often found at some distance from the rest of the mucosa.

*Salpingitis,* other than pyosalpinx, occurred in the tubes as follows: Acute general salpingitis, 14; subacute and chronic general salpingitis, 52.  In other tubes the process seemed limited as follows: Endosalpingitis alone, 23; perisalpingitis, 22;

interstitial salpingitis, sometimes associated with a perisalpin-
gitis, 9. Two cases of chronic salpingitis were tubercular and
have been already mentioned. In the examination of these cases,
as well as those of the pyosalpinx, the origin of certain epithe-
lial formations in the wall of the tube was sometimes doubtful,
but they could usually be recognized as belonging to one or
other of the following conditions: (a) Diverticula from the mu-
cosa, especially in cases of pyosalpinx. In several cases these
were seen to be accessory ostia to the tube, while in others they
probably represented the so-called perisalpinx, i.e., a more or less
complete lumen lying alongside the main mucosa. Very fre-
quently they could be seen to be due to sharp convolutions of
the tube, as a result of which there seemed to be two, sometimes
three, distinct and well-formed lumina. (b) Another source
was from peritoneal inclusions which presented a most varied
appearance, forming cystic spaces lined by single or multiple
layer of epithelium varying in form from the flat to the columnar
type or as solid masses of cells. (c) A third source was from the
Wolffian ducts, so often seen in the mesosalpinx as small tubules
or cysts, but occasionally these occurred in the wall of the tube,
and in one instance in the muscularis on the dorsum of the tube
were found what seemed to be Wolffian ducts.

In connection with the perisalpingitis in four instances there
occurred psammoma formations similar to that mentioned under
perioöphoritis. Two of these cases were associated with papil-
lomatous tumors of the ovary; in two others these bodies were
found in the mucosa of the tube.

A *normal* condition was found in 40 tubes, most of which had
been removed in case of hysterectomy for uterine myomata.
Others were removed with the ovary where the latter was dis-
eased, as in ovarian cysts; 22 tubes showed merely an acute
hyperemia, due probably to traumatism at the operation. They
were removed for conditions similar to those mentioned when
speaking of normal tubes.

*Vagina.*—The following conditions were found: Vaginitis, 2;
epithelioma, 2; normal vagina, 4. The vaginal mucosa removed
by denudation in perineorrhaphy was rarely examined.

*Vulva.*—Tissue from vulvo-vaginal abscess of Bartholin's
gland, 1; condylomata, 1; syphilitic elephantiasis, 1; adenopapil-
loma of labium minus, 1 (this last had an ulcerated surface and
was formed of narrow tubules, suggesting a sudoriferous origin);
cyst of labium minus, 1—this was pedunculated, 1.5 centimetres

in diameter, and lined by a single layer of columnar epithelium.

*Breast.*—Two intracanalicular adeno-myxo-fibromata were examined: one measuring 6.5 x 5 x 3.5 centimetres and weighing 55 grammes; the other measured 3 x 3 x 2 centimetres. They were removed in conjunction with other operative measures.

*Appendix.*—This was removed in 76 cases as a supplementary procedure to some other abdominal operation. The following conditions were found:

Normal appendices, 49. Most of these were removed on account of light adhesions, sharp flexures, etc.; microscopically, however, the appearances were normal.

Total occlusion, 13. As this frequently occurs after middle life, it might almost be included with the normal cases.

Foreign bodies and concretions were found in 5; one of these containing two grape seeds, in the other 4 were hard concretions of débris, epithelium, etc.

Cystic appendices, 2. In one of these, above a constriction, there was a dilated area, 1 centimetre in diameter, lined by a single layer of columnar epithelium. The tubular glands had disappeared from being stretched out flat; the stroma of the mucosa and the lymph nodules were almost entirely gone. The other cystic case was due to myxomatous degeneration of the mucosa and the submucosa.

Myxomatous degeneration of the mucosa occurred in one other case.

Periappendicitis was found 5 times, once in connection with a marked interstitial inflammation, and in another case with an unruptured abscess of the appendix occurring with bilateral pyosalpinx.

A *lipoma* of the shoulder measuring 8 x 5 x 2.25 centimetres was removed at the time of a pelvic operation.

A thrombosed *varicose vein* of the leg was also removed.

Tissues showing *proctitis*, 2; *omentitis*, 9; *papilloma of anus*, 1; *abdominal sinus wall*, 2; *ischio-rectal sinus wall*, 1; *hemorrhoidal tissue*, 1; *pelvic abscess wall removed by vaginal puncture*, 6, were also examined.

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THE ANATOMICAL FINDINGS IN THE HYPO-
PLASTIC GENITALS FROM TWO TRUE
FEMALE DWARFS.

# THE ANATOMICAL FINDINGS IN THE HYPOPLASTIC GENITALS FROM TWO TRUE FEMALE DWARFS.

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The investigation of the two following cases was undertaken at the suggestion of Professor Chiari, as there appeared to be no record of any systematic histological examination of such a case. In fact, after a careful search, there can be found very few histological details concerning uteri of the types of uterus fœtalis, the uterus infantilis, and the uterus hypoplasticus. The first two of these are so similar that it is often difficult to say to which of them a given case belongs. Pozzi says that the distinction is a refinement of anatomy, and that really no difference exists between them, but, as most writers classify them separately, a brief description of each must be given.

By uterus fœtalis we understand one that has developed normally until the date of birth, or, according to v. Winckel, until any period between the twentieth and fortieth week of intra-uterine life. By the twentieth week the Müllerian ducts have become united as far as the fundus uteri, and the intervening septum has completely disappeared; hence, cases showing malformations, such as undeveloped cornua, intra-uterine septa, occlusion of the cavity, etc., cannot properly be included in this category. The cervix is much better developed than the corpus, and on cross section shows a circular form. The cervical mucosa is well formed and shows numerous plicæ palmatæ. The portio is relatively large. The corpus is small, representing as little as one-half, one-third, or even one-quarter of the length of the cervix; its mucosa usually shows plicæ palmatæ, reaching to the fundus, and similar to those in the cervix. The corpus is flattened from before backward, and is, as a rule, sharply anteflexed; its walls are thin and relaxed. The ovaries are small and contain primary follicles, or even Graafian follicles to the period of ripeness (Nagel), sometimes the ovaries are only rudimentary (Säxinger). The tubes are small and delicate but normal; the lumen is patent; frequently they show a persistence of the spiral convolutions described by Freund as occurring at an earlier stage. The vagina and external genitalia are usually normally formed but small.

The uterus infantilis represents a further stage of development, such as occurs between birth and puberty; the size is slightly increased, but it is less than in the normal adult virgin; the corpus is flattened from before backwards, and its walls are thicker; the anteflexion is not so marked; the cervix is still larger than the corpus, but not to such a degree as in the uterus infantilis; in the corpus the plicæ palmatæ have partly or wholly disappeared.

By many writers (Kussmaul, Kleinwächter, and others) a further class has

been constituted, including those uteri that are more advanced in development than the uterus infantilis, but which are still below the normal size at puberty. Such a uterus is of normal appearance, but of small size; the cervix is no longer markedly larger than the corpus. To this class has been given the name of uterus hypoplasticus; it corresponds with the uterus pubescens of Puech, congenital atrophy of Fritsch, or the primary atrophy of Schröder. But, as Virchow, Müller, and Thorn pointed out, this is not a true atrophy at all, but a hypoplasia.

With all the above forms there may be perfect development of the rest of the body, more frequently undeveloped mammæ and an infantile pelvis are found; there may be a general arrest of growth, as in the cases we describe; there may be cretinism, or there may be some constitutional disease, such as tuberculosis or chlorosis; this latter being often associated with hypoplasia of the aortic system, as pointed out by Virchow. Menstruation is usually absent. In eighteen cases recorded by Las Casas dos Santos, three had regular but scanty periods, three were irregular, and with the remaining twelve there was complete amenorrhœa. Pregnancy is possible but very improbable, an abortion usually results even where conception occurs. Stone, however, mentions an instance of infantile uterus, in which a normal delivery at term followed an abortion. Beer calls attention to the frequency of eye lesions in these cases of undeveloped uteri with amenorrhœa, Kussmaul describes the gross appearances of these various forms, and quotes in detail a large number of cases.

For the purpose of forming a correct opinion of the microscopic condition in our two cases, the genitals from a number of other women were examined in a parallel manner. These included virginal organs of the same age as the younger of the two dwarfs; some of these were normal, while others showed various degrees of hypoplasia. Other genitals, corresponding in age with the older dwarf, were also examined. From each uterus a continuous strip from the anterior wall, extending from the fundus to the vagina and including the whole thickness of the uterine wall, was removed; for the sake of convenience this was subdivided into several consecutive pieces; sections from all the ovaries were examined, and also, in most of the cases, from the Fallopian tubes and round ligaments. The sections were stained with Delafield's hæmatoxylin, hæmatoxylin and eosin, Weigert's fuchsin-resorcin stain for elastic tissue, and van Gieson's picric-acid-fuchsin stain, the last being most useful for differentiating the unstriped uterine muscle from the connective tissue; in the examination of the elastic tissue, in some of the cases, controls were made with the Unna-Taenzer method with orcein, but practically similar results were obtained as with Weigert's stain.

The following is a brief review of the literature concerning the normal histological structure of the female genitalia from the fœtal period up to puberty.

Maudach's work especially concerns the persistence of the Wolffian ducts in the uterine wall between the ages of 1 and 16 years; he also describes the appearance of the mucosa, that of the corpus being poorly developed and showing but few glands until the age of 10. The cervical mucosa is well formed at birth, frequently presenting a polypoid appearance at the os internum, where it acts like a valve and causes retention of secretion in the corpus. He believes that the dividing line between the stratified squamous epithelium of the portio and the columnar cervical epithelium is not usually sharply marked; occasionally he found islands of stratified epithelium in the cervical canal.

Roesger deals with the development of the muscularis and the muscle of the vessels of the uterus; while the disposition of the muscle bundles is fairly simple at an early stage, after the beginning of the ninth month of pregnancy

Meyer contributes an article on the fœtal uterine mucosa, in which he ascribes the plicæ palmatæ of the corpus to the more rapid growth of the mucosa as compared with the muscularis in the earlier stages of development.

Grapow says that the plicæ palmatæ are richest at the os internum, and are found also in the corpus until the fifth year. The tube until the thirty-second week of intra-uterine life shows the spiral twists mentioned by Freund. The cervix at birth is almost fully formed, hence its large size as compared with the partly developed corpus. In senility the atrophy is more marked in the cervix and portio; at this period, therefore, the corpus is larger than the cervix, and the relation between the two is the reverse of that in infancy.

Friedländer examined a large number of uteri from children, and concludes that in the first five years the increase in size of the organ is but slight, and is practically limited to the cervix; the cervical mucosa often forms a papillary structure at the os internum, and in 30 per cent. of cases leads to obstruction and retention of secretion in the corpus, where it aids in smoothing out the plicæ palmatæ. During this period the ovaries remain almost stationary. In the second five years the corpus grows more rapidly, especially the muscularis; the mucosa, developing more slowly, is stretched, and this aids in effacing the plicæ; the ovaries increase in size during this time. In the third five years the corpus rapidly increases to its normal size.

Wyder concludes that the development of the corporeal mucosa is slight between the ages of 1 and 15, and during this period it varies in different individuals, the thickness being from 0·5–1·5 mm., the average being about 0·7 mm. About puberty the growth of the mucosa becomes more rapid, and the normal condition is reached in a comparatively short time; he also thinks that the disappearance of the plicæ is due to the more rapid growth of the muscularis. The cervical glands show great variability; as a rule, they are well developed, but in some normal cases they may be very scanty or entirely absent.

Moricke states that the cilia do not occur upon the epithelium until puberty, and are lost in old age; he also says that the stratified squamous epithelium of the portio in children may extend some distance up the cervical canal, and that the plicæ palmatæ of the cervix may not reach the os externum as they usually do in adults.

Dührssen divides the portio into an internal part, surrounding the cervical canal and containing muscle but no elastic tissue, and an external segment with no muscle and two networks of elastic tissue, a subepithelial layer, and a deeper one encircling the vessels. Both layers are continuous externally with similar ones in the vaginal wall. In the new-born, or in the undeveloped uteri, the deeper of these two networks is very poorly developed or absent.

Dittel's work is a continuation of the above; he describes the subperitoneal elastic layer of the corpus as a continuation of the subepithelial layer of the portio.

Buchstab gives the distribution of the elastic tissue in the Fallopian tube from infancy onward; it gradually increases in amount until the maximum is reached between the ages of 21 and 45. In senility it again diminishes; at all periods it is most abundant subperitoneally, and only after the fourteenth year is it found in the mucosa.

Freund discusses the relation between the spiral convolutions of the tube in early intra-uterine life and its subsequent pathological conditions.

Clarke describes, very completely, the development and life-history of the ovary, especially as regards its blood vessels.

## DESCRIPTION OF CASES.

CASE 1.—Specimen No. 5300 B, in the museum of this institute, consists of the external and internal genitals, with the bladder and urethra, from a

female microcephalic true dwarf, æt. 23, a native of India, who died of croupous pneumonia, 12th February 1901. The body measured 112 cms. in length. The skeleton, which is also in the museum (with the exception of the cranium, which shows microcephalus in a high degree, measuring but 29·5 cms. in horizontal circumference), presents the appearance of that of a normal child. The relation between the other bones is normal; the epiphyses of the long bones are still separated from the shafts by cartilage.[1] The history was not available.

The genitals present the following appearances :—The labia majora are deeply pigmented, and on them are a very few fine black hairs; the labia minora and clitoris are small; the hymen is ruptured, and in its place are found a number of caruncles; the vaginal orifice measures 3·7 cms. in internal circumference; the vagina, which has been opened anteriorly, measures 6 cms. in length along the posterior wall, the maximum internal circumference is 5 cms.; the surface shows numerous fine rugæ; the portio vaginalis is well-defined but small, it projects but slightly into the vaginal vault; the anterior fornix is shallow; the posterior is 0·7 cm. deep; the surface is smooth and regular. The whole uterus measures 3·5 cms. in length, 2 cms. in its maximum width, and 1 cm. in thickness. The cervix is 2·5 cms. long, and its wall is 0·5 cm. thick; the os externum is very narrow and untorn; the os internum is not sharply defined; well-marked plicæ palmatæ are seen in the mucosa. The corpus is smaller than the cervix, measuring but 1 cm. in length; the wall is 0·5 cm. in thickness, and rather soft; the vessels are very small; from above the fundus is convex from side to side; the mucosa is very thin and shows a few longitudinal folds continued upward from the cervix; the adnexa are small but perfectly formed, both tubes are patent and delicate in structure; the left is rather convoluted in the outer half, and measures 5 cms. in length; the right tube is 6 cms. long. Both ovaries are small and perfectly smooth upon the surface. On section no Graafian follicles are seen; the right measures 1·3 × 0·7 × 0·5 cm.; the left 1·5 × 0·7 × 0·5 cms. In both ligamenta lata, tubules from the parovarium can be seen; the round ligaments are very thin.

This uterus would therefore agree with the foregoing description of the uterus infantilis; the cervix is well formed, and considerably longer than the corpus; the plicæ palmatæ in the corporeal mucosa are but slightly marked, and less so than we should expect in a uterus foetalis.

The microscopic appearances are as follow :—In the *corpus* the mucosa, which measures about 0·7 mm. in thickness, is fairly well defined from the underlying muscularis; surface epithelium is almost entirely absent, that present forming a single layer of normal columnar cells. Cilia cannot be seen; this may be due to the method of hardening—in alcohol—or to the fact mentioned by Moricke, that they are not found at the stage of development which this organ has reached. The glands are not so numerous as in an adult virgin uterus, but in relation to the thickness of the mucosa their number is about normal; the glandular epithelium is similar to that seen upon the surface and are of normal appearance. The stroma of the mucosa is rich in cells; the vessels are small and few in number. The muscularis is very thin, measuring about 3·5 mm.; it consists of bundles of unstriped muscle with intervening septa of connective tissue; from these latter, fine prolongations extend into the muscle bundles, subdividing them into smaller groups of cells, and very frequently encircling the single muscle fibres. This differentiation of the two tissues is readily made out by means of van Gieson's stain; the individual

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[1] Demonstrated by Professor Chiari before the Verein deutscher Aerzte in Prag, March 8, 1901, *vide Prag. med. Wchnschr.* 1901. No. 14.

muscle cells appear to be perfectly normal in staining reaction and size, although in the outer part of the wall they appear to be slightly plumper. Upon careful measurement, with an eye-piece micrometer, they nowhere appear to be smaller than in the normal virgin uteri among our comparative cases; the relative proportion between the muscle and connective tissue is nearly normal, or at most there is but very slight increase in the amount of the latter. The direction of the muscle bundles is complex, but externally the longitudinal bands seem to predominate, while internally there seems to be a more circular arrangement. About the centre of the wall is a layer rather richer in connective tissue, and here are found the larger vessels, which are relatively of normal size and appearance. Elastic tissue is found in the vessel walls, and a scanty distribution of delicate fibrils is found in the connective-tissue septa in the outer part of the wall. In this situation no well-defined subperitoneal network can be demonstrated; no elastic tissue is found in the mucosa except in the vessel walls. As seen under the microscope, the *cervix* is not sharply defined from the corpus, the surface epithelium in the vicinity being missing; the glands are also absent. The only change to be seen is a gradual increase in the density of the stroma of the mucosa with diminution of the cellular elements. The surface epithelium is present in small amount, and in some places forms a single layer of atypical, rather low, columnar cells, somewhat like those found in the corpus; in other places it is stratified; the cells are cuboidal but very irregular, and their outlines are indefinite; the basal layer is irregular, and the superficial layers are not flattened. The glands are very few and small; the epithelium is irregular, usually cuboidal, and rarely approaches the normal cervical type, frequently it is desquamated and is seen lying in the lumen; the stroma is dense and shows but few vessels. The muscularis is similar to that of the corpus, but in the lower part of the cervix the connective tissue gradually increases; the elastic tissue is found in the vessel walls, and a few delicate fibrils are seen in the connective tissue near the peritoneal surface. The portio presents but a small amount of normal stratified squamous epithelium, the rest having been lost. Beneath it is found a slight cellular infiltration with lymphocytes. Muscle fibres, except in the vessels, are seen in very small numbers, and surrounded by the rather dense connective tissue of which this part is composed. The vessels are few in number; elastic tissue is seen in them as a poorly developed network of fibres immediately beneath the surface epithelium; deeper down but few fine fibres are present; no well-defined layer, such as occurs in normal adult cases, is seen. This agrees with Dührssen's observations on the uteri of children and in a case of uterus infantilis.

The *ovaries* show no germinal epithelium upon the surface; the tunica albuginea is well developed and richly cellular; the cortex is crowded with large numbers of primary follicles containing ova, often closely grouped in nests and separated by very little connective tissue; one or two follicles show a thickening of the zona granulosa, but none are found approaching the size of those at maturity. The medulla shows one or two very small corpora fibrosa. The vessels are not tortuous; elastic tissue occurs only in the vessel walls. The *tubes* were not examined microscopically, but presented the macroscopic appearances normal in a child.

The examination of this case, as compared with normal adult virgin uteri, would therefore show a general quantitative deficiency in the tissues, accompanied by some minor details which may also be found in the uteri of children. The corporeal mucosa, although thin, is well formed; it shows numerous glands, and, considering the size of the whole organ, may be regarded as normal. The cervical glands are few and small, but Wyder shows that great variability in their number is

found in children, whilst in older cases they are often scanty; thus, we have found in a 33-year old virgin, with intact hymen and a normal, or but very slightly hypoplastic, uterus, 5·25 cms. in length, that the cervical glands are almost as few in number as in the above case; the epithelium is lower than usual, but the plicæ palmatæ are well marked. In a 20-year old virgin with intact hymen and distinctly hypoplastic uterus, measuring 4 × 2 × 0·75 cms., the cervical glands are also very scanty, the epithelium being atypical; the superficial epithelium in the cervix is stratified and similar in appearance to that in the case we have described. In a 19-year old nullipara with a normal uterus the glands were very few in number and the epithelium low. Stratified epithelium in the cervical canal may occur in children as an extension upward of the "portio" epithelium (Moricke), but in our case the two kinds of epithelium are not at all similar in appearance. Maudach describes this stratification of the epithelium in normal cases, and its occurrence under pathological conditions has been recognised by Ruge and Veit, Gebhard, Küstner, Friedlander, Zeller, and others. This stratification was found in the 20-year old virgin, as mentioned above, and in a 65-year old multipara. The relation between the muscle and connective tissue in the uterine wall is normal or with but a very slight increase in the latter; the individual muscle cells are normal; the elastic tissue is small in amount but normal for children; in the 20-year old virgin the amount was even less. The ovaries are typically those of a child.

CASE 2.—Specimen No. 4607 D, in the museum of this Institute, consists of the genital apparatus from a true dwarf, æt. 74 years, who died in the Allgemeines Krankenhaus, Prag, June 8, 1891. The tissues were fixed and preserved in alcohol. The history, as kindly furnished by Professor von Jaksch, shows that she had developed normally until 10 years of age, when her growth had ceased; details of her sexual life, as regards menstruation, etc., and of diseases in childhood, were not obtainable. The clinical diagnosis was as follows:—Catarrhal bronchitis, chronic nephritis, œdema of the feet, and slight acute dropsy. The autopsy was performed in this Institute, the anatomical diagnosis being:—*Morbus Brightii chronicus cum atrophia renum, Hypertrophia cordis ventriculi sinistri gradus levis, Degeneratio myocardii adiposa, Endarteritis chronica deformans, Tuberculosis obseleta apicum pulmonum, Nanosomia, Hypoplasia apparatus genitalis.* The following extracts are made from the autopsy report:—The body measures 122 cms. in length; the bony structure is small, as in a child, but it is well proportioned; the muscles are poorly developed; the mammæ are undeveloped, the nipples being small and but slightly pigmented. The heart is small, with slight hypertrophy of the left ventricle; distinct scattered yellowish areas are seen in the myocardium; the valves, in size, resemble those of a child's heart; the aortic and bicuspid valves are thickened in places. The aorta, just above the valves, measures 6 cms. in internal circumference; at the beginning of the descending aorta it is 5 cms.; in the wall can be seen endarteritis chronica deformans, which is also present in the larger vessels. In the apices of both lungs is found old pigmented scar tissue. The kidneys are of small development and shrunken; on the surface are numerous scars and a number of yellowish spots; the substance of both is dense and the cortex in places measures only about 2 mm. in

is small and infantile; between the shaft of the right femur and the epiphyses, at both upper and lower ends, there is bony union, but upon the surface the line of junction can be plainly seen; on all the vertebræ the line of union is visible between the epiphyses and the bodies. On the sternum the lines of union can be seen between the manubrium and corpus, between the corpus and processus xiphoides, and also a third line is seen across the corpus at the level of the insertion of the third ribs.

The specimen consists of the internal and external genitals, the bladder, and urethra. The labia majora, labia minora, and clitoris are all small; the hymen is intact, forming a concentric fold situated posteriorly; the orifice measures 0·75 cm. in diameter. The vagina has been opened posteriorly; the anterior wall is 5 cms. in length; the internal circumference of the vagina is 3·5 cms.; the rugæ are well marked; the portio is small; the anterior lip is almost flush with the vaginal wall and forms a smooth strip 0·3 cm. wide; the posterior lip is also smooth and projects into the vaginal vault 0·35 cms. The whole uterus measures 3·5 cms. in length; the greatest width is 2 cms., and the thickness of the uterus is 0·6 cm. The cervix, 2·5 cms. long, is well developed; the wall is 0·3 cm. thick; the plicæ palmatæ are well marked; the os externum, 0·3 cm. in transverse diameter, is untorn; the os internum is not sharply defined; the corpus is very small and flattened. The fundus is convex transversely; the wall, 0·3 cm. thick, is soft; the vessels are very small; the mucosa is quite smooth and very delicate; it shows no plicæ. The ovaries are small, flattened, and perfectly smooth; they are rather elongated in form, and measure 2·0 × 0·5 × 0·4 cms.; the tubes are 9 cms. long, small and delicate; the fimbriated ends are patent. In both ligamenta lata can be seen parovarian tubules; the round ligaments are delicate. The urethra and bladder are small but normal.

*Microscopically,* the superficial epithelium of the mucosa in the *corpus* is almost entirely lost; where present, it forms a stratified layer of irregular cuboidal cells with indefinite outlines; the glands are almost completely missing; one or two of small size are seen, and these have a single layer of normal columnar epithelium. Cilia cannot be seen either here or upon the surface; the stroma is dense and not well defined from the muscularis; the mucosa is very thin, measuring 0·2 mm.; the muscularis is also thin and consists of bundles of muscle cells running in various directions; between these are well-marked connective-tissue septa, from which finer prolongations extend between individual muscle cells or between groups of two or three. No regularity of direction of the muscle bundles is apparent; the proportion of connective tissue to the muscle, when compared with normal virgin uteri from younger cases, seems but slightly increased, and it is certainly less in amount than in multiparæ. The individual muscle cells show no atrophy, and by careful micrometer measurements appear to be of the same size as in virgin uteri; the vessels are rather few in number, and proportionately are of normal size and appearance. In the corpus elastic tissue occurs in the vessel walls, and delicate fibres are found in small numbers in the connective tissue of the outer part of the uterine wall; a well-defined subperitoneal network cannot be seen, and the amount is below the normal. In the *cervix* the superficial epithelium of the mucosa resembles that in the corpus, and is composed of stratified irregular cuboidal cells without definite outlines. The glands are few and small; in but one or two places does the epithelium approach the typical form; usually, it forms a single layer of irregular cuboidal cells with indefinite outlines. The stroma is dense; near the os externum it shows a slight grade of lymphatic cellular infiltration. The muscularis is similar to that found in the corpus, but the proportion of connective tissue is slightly greater in the lower part of the cervix; elastic tissue is found in the vessels, and small numbers of fine fibrils in the connective tissue; a continuation of the subepithelial network of the portio is prolonged for some distance beneath the stratified epithelium

found in the cervical canal. The *portio* epithelium resembles that found in the corpus and cervix; it is irregular, stratified, and does not show the usual definite outlines. In one or two places it is reduced to a single layer of cuboidal cells; muscle fibres, except in the vessel walls, are almost entirely absent; a few isolated fibres are seen here and there. Elastic fibres form a well-marked subepithelial network, but a deeper layer is not seen; a few fine fibres occur in the connective tissue, in the inner as well as the outer part of the portio. The *ovaries* have lost the germinal epithelium upon the surface; the tunica albuginea is relatively thick and is composed of interlacing bundles of dense fibrous tissue; the cortex is thin and shows no follicles; a few small spaces, containing a granular débris, however, suggest degenerated primary follicles. The medulla contains numerous well-preserved vessels, which are not unduly thickened; two small cystic spaces, just visible to the naked eye, appear to be of parovarian origin; a few small hyaline corpora fibrosa are found; elastic tissue occurs only in the vessels. The *tubes*, of normal macroscopic appearance, were not examined.

Since the age of this dwarf was 74, not only must the question of an original hypoplasia be considered but also that of senile atrophy. The macroscopic appearance does not suggest a mere senile atrophy, since, with such, the diminution in size occurs mainly in the portio and cervix, while in this case these are relatively large as compared with the corpus. The corpus mucosa is extremely thin, more so than in any other case examined; the glands are very few in number; this may represent a senile change, but the glands present are well formed and none are found in process of obliteration. The cervical glands are also scanty and small, and their epithelium is rarely typical. As previously mentioned this may occur in children and also at times in normal adults; it is not, therefore, a proof of senile atrophy. The occurrence of stratified epithelium in the cervical canal has been discussed under the former case; here it occurred also in the corpus. The muscularis is very thin, but thicker than in the 20-year old virgin above referred to. It shows a very slight increase of connective tissue, but less than we found in multiparæ; the appearance is very similar to that in the other dwarf. No atrophy of the protoplasm of the muscle cells, as described by Lilienfeld after castration, can be seen; the amount of elastic tissue resembles that in the former instance; it shows no degeneration, such as Dührssen describes in senile cases, and which was well seen in a 65-year old and an 85-year old multipara. The naked-eye appearances of the ovaries are those of the ovaries of a child. Microscopically, the vessels show no senile change; the disappearance of the follicles may be due to old age, or it is possible that originally the number was small; the surface of the ovary is smooth and without scars. Clarke shows, however, that maturation and then retrogression of the follicles may occur without rupture; this process is analogous to the formation of the corpus luteum, and would account for the small hyaline corpora fibrosa found in the medulla.

From the naked-eye appearances of these two uteri, especially the

large size of the cervix of each as compared with the corpus and the absence of well-marked plicæ palmatæ in the corpus, they would correspond with the uterus infantilis. The histological examination reveals a pure hypoplasia, part of the general dwarfing; no true atrophy is evident, although in the older case it may account for the thinness of the mucosa and the absence of ovarian follicles; the muscularis closely resembles that of the uterus of adult virgins, but is less in amount, while the mucosa is similar to that described by several writers as occurring in the uteri of children.

## REFERENCES.

ANDREWS . . . . . . . "Malformations of the Uterus," *Am. Gynæc. and Obst. Journ.*, N.Y., 1900, vol. xvi. p. 442.

BEER . . . . . . . . "Ueber einen Fall von Sehnervenaffection bei Uterus infantalis," *Wien. klin. Wchnschr.*, 1892, Ss. 435, 465.

BUCHSTAB . . . . . . "Das elastische Gewebe in den Eileitern der Frauen," *Centralbl. f. Gynäk.*, Leipzig, 1897, Bd. xxi. S. 896.

CLARKE . . . . . . "The Blood Vessels of the Human Ovary," *Johns Hopkins Hosp. Rep.*, Baltimore, 1900, vol. ix. p. 593.

DIRNER . . . . . . "Ueber Behandlung der Sterilität bei angeborner Kleinheit des Uterus," *Verhandl. d. deutsch. Gesellsch. f. Gynäk.*, Leipzig, 1895, Congr. 6, S. 832.

DITTEL . . . . . . . "Ueber die elastischen Fasern der Gebärmutter," *Wien. klin. Rundschau*, 1896, Bd. x. S. 445, 465.

DÜHRSSEN . . . . . . "Beitr. z. Anat. Physiol. u. Pathol. der Portio vaginalis uteri," *Arch. f. Gynaek.*, Berlin, 1891, Bd. xli. S. 259.

FABER . . . . . . . "Klinisches ueber den Uterus unicornis und infantalis," Dorpat, 1881.

FENYKÖVY . . . . . . "Sterilität in Folge von Vagina u. Uterus infantalis," *Wien. med. Presse*, 1883, Bd. xxiv. S. 1349.

FISCHER . . . . . . "Ueber genitale Atrophie bei innerer Erkrankung," *Wien. klin. Wchnschr.*, 1896, Bd. ix. S. 561.

VON FOSTER . . . . . "Ueber congenitale Hypoplasie des Uterus," Erlangen, 1875.

FREUND . . . . . . "Ueber die Indikationen zur operativen Behandlung der Erkrank. der Tuben," *Samml. klin. Vortr.*, Leipzig, 1888, No. 323 (Gyn. No. 93).

FRIEDLÄNDER . . . . . "Ueber Wachstums-Veränderungen an kindlichen Uteri," *Arch. f. Gynaek.*, Berlin, 1898, Bd. lvi. S. 635.

FRIEDLÄNDER . . . . . "Abnormale Epithelbildungen in kindlichen Uteri," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1898, Bd. xxxviii. S. 8.

GEBHARD . . . . . . "Pathol. Anat. der weiblichen Sexualorgane," Leipzig, 1899.

GEBHARD . . . . . . "Ueber die vom Oberflächenepithel ausgehenden Carcinomformen," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1892, Bd. xxiv. S. 1.

GOTTSCHALK . . . . . "Beitr. z. Lehre von der Atrophia uteri," *Samml. klin. Vortr.*, Leipzig, 1892, No. 49 (Gyn. No. 20).

GRAPOW . . . . . . "Die postfoetale Entwickelung der weiblichen Zeugungsorgane," etc., *Deutsche med. Wchnschr.*, Leipzig, 1890, Bd. xvi. S. 788.

GREENWALT . . . . . "Infantile Uterus," *Am. Journ. Obst.*, N.Y., 1895, vol. xxxi. S. 377.

GRIGG . . . ʻ. . . . "The Infantile Uterus," *Obst. Journ. Gt. Brit.*, London, 1875, vol. ii. p. 699.

HEITZMAN . . . . . . "Uterus membranaceus (Atrophia präcox)," *Wien. med. Presse*, 1884, Bd. xxv. S. 400.

HILLER. . . . . . . "Tiefe Ernährungs und Entwickelungs störungen im Anschluss an Chlorosis," etc., *Charité-Ann.*, Berlin, 1882, Bd. vii. S. 338.

JACQUET . . . . . . "Ueber Atrophia uteri," *Beitr. z. Geburtsh. u. Gynaek.*, Würzburg, 1872, Bd. ii.

JENKS . . . . . . . "Infantile Uterus," *Centralbl. f. Gynäk.*, Leipzig, 1896, Bd. xx. S. 594.

JOHNSON . . . . . . "The Infantile Uterus," *Trans. Am. Gynec. Soc.*, 1887, vol. xii. p. 275.

KEELER . . . . . . "Case of Infantile Uterus and Vaginismus," *Med. Era*, Chicago, 1899.

KLEINWÄCHTER . . . . "Die manglehaft Entwickelung des Uterus," *Wien. med. Presse*, 1899, Jahrg. 40, S. 1993.

„ . . . . "Einige Worte ueber die Atrophie des Uterus und der Ovarien," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1889, Bd. xvii. S. 42.

KLOB . . . . . . . "Pathol. Anat. der weiblichen Sexualorgane," Wien, 1864.

KUSSMAUL . . . . . . "Von dem Mangel der Verkümmerung und Verdoppelung der Gebärmutter," etc., Würzburg, 1859.

KÜSTNER . . . . . . "Notiz. z. Metamorphose des Uterusepithel," *Centralbl. f. Gynäk.*, Leipzig, 1884, Bd. viii. S. 320.

LAS CASAS DOS SANTOS . "Missbildungen des Uterus," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1888, Bd. xiv. S. 140.

LILIENFELD . . . . . "Ueber den anatomischen Befund an dem Genitalapparate einer einunddreissigjährigen Frau nach bilateraler Castration," *Ztschr. f. Heilk.*, Berlin, 1898, Bd. xix. S. 357.

LITSCHKUS . . . . . . "Beitr. z. Frage ueber die Anomalien des Uterus," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1888, Bd. xiv. S. 369.

MACKENZIE . . . . . "Malformations of the Uterus," *Trans. Path. Soc. London*, 1892, vol. xliii. p. 111.

M'GINNIS . . . . . . "Infantile Uterus," *Am. Gynæc. and Obst. Journ.*, N.Y., 1898; *Centralbl. f. Gynäk.*, Leipzig, Bd. xxii. S. 1299.

VON MAUDACH . . . . "Beitr. z. Anat. d. Uterus von Neugebornen und Kindern," *Virchow's Archiv*, 1899, Bd. clvi. S. 94.

MEIGE . . . . . . . . "Infantilisme chez la femme," *Nouv. icon. de la Salpètriére*, Paris, 1895, tome viii. p. 218.

MEYER . . . . . . . . " Ueber die foetale Uterusschleimhaut," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1898, Bd. xxxviii. S. 234.

MILROY . . . . . . "Two Cases of Arrested Development of the Female Genitals," *Kansas City M. Index*, 1894.

MORICKE . . . . . . " Die Uterusschleimhaut in den verschiedenen Altersperioden," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1882, Bd. vii. S. 84.

NAGEL . . . . . . . "Entwickelung u. Entwickelungsfehler der weiblichen Genitalien," Veit's "Handbuch der Gynaekol.," Wiesbaden, 1897, S. 519.

OPPEL . . . . . . . "Anomalien der Grösse des Uterus," *Wien. med. Presse*, 1865, Bd. vi.

POZZI . . . . . . . "Traité de gynécologie," Edition 3, Paris, 1897.

PUECH . . . . . . . " Atrophie de l'uterus," *Gaz. obst. de Paris*, 1874, tome iii.

ROBINSON . . . . . . "Development of the Female Genitals and their Life-History," *New York Med. Journ.*, 1900, vol. lxxi. p. 158.

ROESGER . . . . . . "Zur foetalen Entwickelung des menschlichen Uterus," *Gesellsch. f. Geburtsh. u. Gynäk. zu Berlin*, 1894 ; *Centralbl. f. Gynäk.*, Leipzig, 1895, Bd. xix. S. 53.

RUGE AND VEIT . . . . " Zur Pathologie der Vaginalportion," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1877, Bd. ii. S. 415.

SAVOR . . . . . . . " Rudimentärer Uterus," *Verhandl. d. Geburtsh. u. Gynäk. Gesellsch. in Wien ; Centralbl. f. Gynäk.*, Leipzig, Bd. xxii. S. 1324.

SÄXINGER . . . . . . " Primäre Atrophie des Uterus," *Prag. Vrtljschr.*, 1889.

SCHAUTA . . . . . . "Missbildung des weiblichen Genitales," *Allg. Wien. med. Ztg.*, 1898, Bd. xliii. S. 585.

SCHROEDER . . . . . " Weibliche Geschlechtsorgane," Leipzig, 1886.

SHOEMAKER . . . . . "Malformations of the Female Genitals," *Am. Journ. Obst.*, N.Y., 1895, vol. xxxii. p. 215.

SKENE . . . . . . . " Treatment of Incomplete Development of the Uterus," *Brooklyn Med. Journ.*, 1898, vol. xii.

TAIT . . . . . . . . "Fall von Infantilem Uterus," *Monatschr. f. Geburtsh. u. Gynaek.*, Berlin, Bd. ix. S. 429.

TENNBERG . . . . . . " Beitr. z. Kentniss der angebornen Missbildungen der weiblichen Geschlechtsorgane," *Ibid.*, 1897, Bd. v. S. 300.

THOM . . . . . . . " Beitr. z. Lehre von der Atrophia uteri," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1889, Bd. xvi. S. 57.

VINEBERG . . . . . . " Arrest of Development in Uterus and Ovaries," *Am. Journ. Obst.*, N.Y., 1895, vol. xxxi. p. 525.

   „ . . . . . . . "Premature Atrophy of the Sexual Organs," *Ibid.*, 1894, vol. xxix. p. 513.

VIRCHOW . . . . . . " Ueber die Chlorose und die damit zusammenhängenden Anomalien im Gefässapparate," *Beitr. z. Geburtsh. u. Gynaek.*, Würzburg, 1872, Bd. i. S. 323.

VEIT . . . . . . . "Zur Erosionsfrage," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1882, Bd. viii. S. 77.

WYDER . . . . . . . "Beitr. z. normalen u. patholog. Histol. der menschl. Uterusschleimhaut," *Arch. f. Gynaek.*, Berlin, 1878, Bd. xiii. S. 1.

VON WINCKEL . . . . "Ueber die Eintheilung, Entstehung u. Benennung der Bildungshemmungen der weiblichen Sexualorgane," *Samml. klin. Vortr.*, Leipzig, 1899, N. F., 251 and 252 (Gyn. 90–91), S. 1523.

„ . . . . "Die Pathol. der Weiblichen Sexualorgane," Leipzig, 1881.

ZELLER . . . . . . . "Plattenepithel im Uterus," *Ztschr. f. Geburtsh. u. Gynäk.*, Stuttgart, 1885, Bd. xi. S. 56.

# A CONTRIBUTION TO THE KNOWLEDGE OF OSSIFICATION OCCURRING IN THE EYE, WITH CLINICAL REPORT OF CASES OCCURRING IN THE SERVICE AT LAKESIDE HOSPITAL.

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### HISTORICAL.

Ossification of the various structures of the eye have been reported from time to time for over a century. Little consideration can be given to some of the earlier writings on this subject for two reasons:

First: In numerous cases reported as ossification the diagnosis rested upon the presence of hard masses in the eye, unsupported by histological examinations.

Second: Reports of ossific processes developing in structures of the eye which today we are confident do not occur, such as the lens, vitreous humor, ciliary body, and iris. It is to be regretted that in over one-fourth of the cases we have been able to collect from the literature there is no reference to histological examination, and that in over one-half of the cases reported nothing is said regarding the mode of development of the bone.

Pagenstecker in 1860 was probably the first to write fully upon this subject. Since then Knapp in 1871, Alt in 1877, and Goldzieher in 1880, have discussed the subject very thoroughly. Berthold (1871), Schiess-Gemuseus (1873), Hoene (1882), Fontan (1883), Ried (1892), and Webster (1901), have also touched upon the mode of bone formation in the cases they reported.

The reports of forty-nine cases have been collected from the literature, and of these in only thirty-eight is there more or less satisfactory description of the histological appearances. To

these we wish to add four more cases, making forty-two cases in all in which the diagnosis was substantiated by microscopical examination.

It can scarcely be credited, however, that this condition is not of more frequent occurrence than the literature of the subject would seem to indicate, for the four cases here reported all occurred in Lakeside Hospital service in less than one year.

### CASE I. ·SUMMARY.

I.  Clinical.  Phthisis bulbi, result of injury; sympathetic irritation, tenderness of blind eye.

II.  Pathological.  Chronic panophthalmitis, with ossification of the organized inflammatory exudate posterior to the lens. Detached and degenerated retina.  Atrophied and calcareous lens.  Detachment of the choroid and of the posterior portion of the ciliary body from the sclera.

#### CLINICAL HISTORY.

J. K., male, aet. 25 years.  Was admitted to Lakeside Hospital August 28, 1901, giving the following history:  Eighteen years previously the patient accidentally stuck the point of a pair of scissors into the right eye, producing a serious wound, leading to contraction of the eyeball, a phthisical bulb.  There had been no trouble with the eye until in the spring of 1901, when it became somewhat painful and teared considerably.  The left eye had shown a tendency to tear with some discomfort in the cold weather during two or three winters previously.  For a month before entering the hospital there had been more than usual tearing of his sound eye, with considerable pain at times. For this he went to the Eye Dispensary at Lakeside Hospital, where, under treatment, the discomfort had largely disappeared. The injured eye had been somewhat painful for several months, the pain being of a sharp, shooting character, and as the irritation of the eye did not subside under treatment he was referred to the house for enucleation.  Examination showed the right eye much smaller than the left, the tension diminished, the cornea

entirely opaque, with a transverse scar across its center, the result of the old injury, considerable conjunctival reddening, tenderness on pressure, etc. The eye continued to increase in irritability until on August 31st, when, under general anæsthesia, the eyeball was enucleated. The patient made an uninterrupted recovery and was discharged from the hospital on September 7th.

The eyeball was referred to the pathological department for examination.

### DESCRIPTION OF EYE.

The eye is about half its natural size, irregular in shape, and has its greatest diameter transversely. The cornea is greatly shrunken and opaque, and yellowish white in color. On palpation a hard tumor mass is felt in the interior of the eye. A median antero-posterior section reveals the sclera considerably thickened, especially posteriorly, where it is 2 mm., thick, about twice that in the normal eye. The inner surface of the sclera is yellowish white in color, and in no place does any pigment layer appear to be present. An irregularly oval mass of bone-like consistency occupies about one-half of the interior of the eye. It is attached anteriorly in a position corresponding to the posterior surface of the cornea, the free portion being of a brownish black color. This mass measures 19 x 12 x 10 mm., its greatest diameter being transversely, and least antero-posteriorly. The cut surface of the mass shows a lamellated structure closely resembling that of bone, and at its posterior portion there is a small irregularly round cavity about 4 mm. in diameter. The iris is apparently present between the mass and the posterior corneal surface, these three structures being intimately adherent, obliterating the anterior chamber. The pigment layer is very evidently attached to the outside of the mass for a space of about 3 mm. beyond its attachment to the eyeball, and then rather abruptly becomes thinned and merges into the brownish black covering of the free portion of the mass. The lens cannot be made out. The remaining portion of the eye, which formerly had been filled with vitreous humor, contained a dirty looking sero-purulent material when the eye was removed. A delicate

slightly funnel-shaped mass of tissue its base anteriorly, extends from the region of the optic nerve to the posterior portion of the tumor mass, evidently the remains of the detached retina. Microscopically the whole eye shows evidences of an old inflammation. The sclera is greatly thickened, especially posteriorly. The cornea shows marked change. The corneal epithelium is thinned in some places and in others is entirely absent. There are no evidences of recent inflammation, however. The substantia propria is almost entirely replaced by ordinary fibrous tissue like that of the sclera. The lamellated structure and the nuclei of the cells are either lost or very indistinct. One small area alone shows a dense homogeneous structure, with lacunæ containing stellate corpuscles, resembling normal corneal tissue. The inner surface of the cornea stains more deeply than the rest, but the cell structure of the endothelial lining is entirely lost. The iris is adherent to the posterior surface of the cornea throughout almost its entire length, obliterating the anterior chamber. The iris and ciliary bodies are somewhat atrophied and congested. The choroid and the lower portion of the ciliary body is detached from the inner surface of the sclera and forms a covering to the surface of the tumor mass. Here and there portions of choroidal tissue are included in the tumor mass. It is very unevenly distributed over the tumor and in some places greatly thinned. The retinal tissue seems to have entirely disappeared. Just posterior to the iris is a zone, apparently the result of a fibrinous exudate. This zone is composed of delicate fibrinous strands and contains no cellular elements or blood vessels, and is of moderately loose structure. In the center of this tissue is an irregular mass of dense calcareous tissue staining very dark blue. It is lens-shaped and evidently the remains of an atrophied calcareous lens. Posterior to this loose fibrinous layer is another or denser structure extending almost directly across the eye from the region just back of the ciliary body. This layer consists of interlacing fibrillæ supporting connective tissue cells. The nuclei of these cells are rather irregular in size, and a number of round cells are scattered diffusely through-

out this tissue. A few plasma cells are seen. This tissue is quite vascular. Many of the arteries show a well marked obliterating endarteritis and their coats show marked hyaline degeneration involving especially the media. The posterior portion of this layer is in contact with the bone and is denser than the rest of the layer and contains fewer cellular elements. There is a considerable amount of choroidal pigment here and there through this area. The osseous portion of the tumor is made up of normal spongy bone. The Haversian canals are of good size and contain blood vessels and fat tissue. The lacunæ contain typical stellate bone corpuscles. A few osteoclasts are to be seen. In a few places metaplasia of fibrous tissue into bone can be readily traced, the fibrous tissue becoming denser and less cellular as it approaches the fully developed bone. This dense tissue is largely composed of a homogeneous finely fibrillated matrix, hyaline in character, which here and there encloses spindle and stellate cells. No cartilage is seen.

## CASE II. SUMMARY.

I. Clinical. Phthisis bulbi. Result of old injury. .

II. Pathological. Chronic panophthalmitis, with ossification of the organized inflammatory exudate from the chorio capillaris and partial ossification of the septum. Detached retina. Partly calcareous lens.

### CLINICAL HISTORY.

L. B., female, aet. 17 years. Was admitted to Lakeside Hospital May 1, 1902, giving the following history: When she was one year old the left eye was injured by being struck with a guncap, after which the eye was greatly inflamed and very painful. The eye was left in a phthisical condition with a large scar involving the central portion of the cornea. The eye has never given her any trouble since healing after the injury, nor has there been any evidence of sympathetic irritation. The patient desired the removal of the eye on account of its appearance, so that she might use an artificial eye. Under general anæsthesia

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on May 2d the eyeball was removed.  Recovery was uninter-
rupted and the patient was discharged on May 15th.

### DESCRIPTION OF EYE.

The eye is about half the normal size, irregular and some-
what cubical in shape.  The cornea is opaque.  On palpation
the whole posterior half of the eye is of bone-like hardness.
An equatorial section of the eye reveals the sclera considerably
thickened, the retina detached, except at the optic nerve and ora
serrata, giving it a funnel-shaped appearance.  The anterior
chamber is obliterated and the iris and remains of the lens lie in
close contact with the cornea. · The choroid lies in its normal
position in apposition with the sclera, and just internal to the
former there is a shell of bone-like hardness.  This shell is un-
equally distributed over the interior of the choroid, extending
about to the equator of the eye on one side, and on the other it
extends forward to the region just posterior to the lens and
seems to extend for a short distance into the septum formed by
an organized exudate just posterior to the lens.  This hard plate
is not of uniform thickness, but has a very nodular appearance,
in a few places being over 3 mm. thick, though most of it is 1
to 2 mm. thick.  A small hole in the bony shell is seen where
the retina passes through, and is attached about the optic nerve.
About one-half of the remaining interior of the eye is filled with
a soft cream-colored tissue.  Microscopically the corneal epithe-
lium is somewhat irregular in width, and in a few places is ab-
sent or the cell structure lost.  The substantia propria shows a
slight round cell infiltration in places, and here and there a
few blood vessels are seen.  The cell structure of the endothelial
lining is entirely lost.  The sclera is greatly thickened, es-
pecially posteriorly, and there is some round celled infiltration
in places.  The iris and ciliary bodies show a diffuse round cell
infiltration with some increase of the cellular elements.  The
lens is fibrous with a zone of calcareous material about it.  The
choroid is greatly thickened and congested, and shows a slight
diffuse round cell infiltration, with an increase of the normal

cellular elements. Just internal to the choroid and apparently involving its inner layers is a tissue having a delicate fibrillated structure, supporting spindle and stellate cells, apparently a delicate fibrous tissue. In this tissue there is a shell of true bone with typical bone corpuscles in lacunæ connected by canaliculi. Here and there are small canals apparently rudimentary Haversian systems containing blood vessels and fat tissue. Internal to this layer is a portion of the retina in situ, though it is detached in most of the section and occupies the center of the vitreous chamber. The layer of rods and cones and ganglion cells seems to have entirely disappeared. The nuclear and reticular layers are more or less intact and can be traced in a large part of the section. The nuclear and reticular layers are greatly thickened, and there is a marked proliferation of the cellular elements of the nuclear layer throughout the section. Just posterior to the lens a mass of tissue extends across the eye from the region just posterior to the ciliary body. It is a direct continuation of the tissue just internal to the choroid in which the ossification has taken place and is identical structurally. Here and there throughout the section are areas of tissue situated between the bone and the loose fibrous tissue which demonstrate the metaplasia clearly. The loose connective tissue gradually becomes denser as it approaches the bone. The cellular elements become scattered and few in number, due to an increase in the interstitial tissue. This tissue becomes very dense and hyaline in character, with a delicate fibrillated structure enclosing here and there the stellate connective tissue cells. In places the branches of the cells may be seen invading the homogeneous matrix, and the whole picture resembles that of true bone with its bone corpuscles and canaliculi except for the deposition of lime salts.

<div align="center">CASE III. SUMMARY.</div>

I. Clinical. Phthisis bulbi. Result of old injury. Sympathetic irritation.

II. Pathological. Chronic panophthalmitis, with ossification of the organized choroidal exudate forming a partial shell

of bone. Septum not ossified. Detached retina. Calcareous
lens surrounded by organized inflammatory exudate.

## CLINICAL HISTORY.

S. D., female, aet. 39 years. Was admitted to Lakeside Hos-
pital May 22, 1902. She gave the history that at three years of
age she was struck in the left eye with a stick, since which time
she had been unable to see with it. From the history it would
seem that the right eye must have had some sympathetic irrita-
tion afterward, as she states that for several weeks succeeding
the injury she was unable to see anything clearly with it. The
vision in the right eye improved slightly, so that at eight years
of age she thought she was as well as ever. Until six or seven
weeks before entering the hospital she had had no trouble since
eight years of age. At this time she was attacked with a sharp
pain in the right eye, with dimness of vision, which was continu-
ous up to the time of admission to the hospital. Examination
at the time of admission gave the following result: O. D. V.=
6/18-2. There was some redness of the conjunctiva of O. D.,
but no tenderness on pressure. T.=n. Ophthalmoscope
showed the pupil of O. D. good size, responding promptly to
light, fundus somewhat hazy, so that the details were made out
with great difficulty, but apparently no marked pathological
changes. The left eye showed a phthisical bulb, sensitive on
pressure, with a hard feeling as though a calcareous deposit ex-
isted. The patient was sent to the hospital for enucleation.
This was done on the afternoon of May 22d. The patient made
an uninterrupted recovery and was dismissed from the hospital
on June 2d.

On June 12th an examination of the right eye was made, the
vision being slightly subnormal. With a —1.50 Ds. it was
6/12.

## DESCRIPTION OF EYE.

The eye is about half the normal size, and somewhat irregu-
lar in shape. The cornea is opaque. On palpation the posterior
third of the eye is of bone-like hardness. A median antero-pos-

terior section reveals the sclera somewhat thickened posteriorly. The anterior chamber is obliterated, the iris lying in close contact with the cornea. The lens is hard and apparently calcareous, lying just behind the iris. Just inside the choroid, which was in normal position, is a hard shell lining about a third of the posterior portion of the eye about the optic nerve. This shell is of fairly uniform thickness, being about 1 mm. thick throughout. A small aperture exists about the middle of this bony plate, where the retina passes through and is attached posteriorly about the optic nerve. The retina is detached except in the region of the optic nerve and the ora serrata. A portion of the vitreous chamber is filled with an organized exudate which is most marked anteriorly just posterior to the lens, where it extends across the eye like a septum, being attached laterally to the choroid just posterior to the ciliary body. Microscopically the corneal epithelium is lost in places. The substantia propria is almost entirely replaced by ordinary fibrous tissue. The endothelial lining is lost. The iris is adherent to the posterior surface of the cornea. Here and there is a well marked fibrous tissue, thickening, though the greater part of the iris is atrophied. The remains of the lens consists of an atrophied and calcareous shell which lies just posterior to the iris in a delicate tissue of fibrillated structure containing a few connective tissue cells. The ciliary body is negative. The outer layer of the choroid is very vascular and thickened in places. On the inner surface of the choroid is a layer of tissue similar to that described about the lens. This tissue covers the whole surface of the choroid in a moderately thin layer, and extends across the eye posterior to the lens as noted above. Posteriorly about the optic nerve and extending over about half the eye is a shell of bone lying in this tissue. This shell occupies nearly all of the delicate tissue previously spoken of. This bone is intersected by numerous Haversian canals containing blood vessels and fat tissue. The lacunæ and canaliculi have a somewhat definite concentric arrangement. Near the extremity of this bony shell the process of ossification is readily traced. The denser tissue with its delicately fibrillated structure is in places somewhat granular looking, always inter-

vening between the completely formed bone and the loose fibrous tissue.

## CASE IV. SUMMARY.

I.  Clinical.  Phthisis bulbi.  Result of injury.  Recurring attacks of inflammation.

II.  Pathological.  Chronic panophthalmitis, with osseous masses in the organized choroidal exudate.  Retina and lens have disappeared.  Osteoid looking tissue at the base of several ciliary processes.

### CLINICAL HISTORY.

Male, aet. 47.  Injured O. S. three years ago.  Eye sightless and he has had recurring attacks of inflammation in it at times since the injury.  No symptoms of sympathetic irritation.

### DESCRIPTION OF EYE.

The eye is not half the normal size.  Very irregular in shape and flattened antero-posteriorly.  The cornea is opaque.  On palpation the posterior portion of the eye is of bone-like hardness.  A median antero-posterior section reveals a greatly thickened sclera, especially posteriorly.  The anterior chamber is obliterated.  The iris is in close contact with the cornea, and just posterior is the shrunken lens, which appears calcareous.  The choroid is in the normal position, and just internal to it is a layer of soft tissue in which is a small shell of extremely dense substance almost 1 cm. in diameter.  The eye is so shrunken that the vitreous chamber is very small and almost entirely filled by this soft tissue.  A mass of this tissue projects through the vitreous chamber, forming a septum just posterior to the lens from the region just behind the ciliary body.  This septum becomes rapidly thinned toward the center of the eye, being broadest at its attachment in the ciliary region.  No retina made out.  Microscopically the corneal epithelium is lost in places.  The substantia propria is entirely replaced by ordinary fibrous tissue with well marked round cell infiltration in places.  The endothelial lining is lost in places, the cells proliferated in others.

The sclera is vascular and greatly thickened posteriorly. The
iris is thickened and shows a diffuse round cell infiltration. The
connective tissue cells are large and abundant. The vessels are
markedly congested. The iris is not in close contact with the
cornea, but separated from it by a layer of structureless hyaline
material which is also seen on the posterior surface of the iris.
The ciliary bodies show congestion and round cell infiltration.
Just at the base of the several ciliary processes are small areas
which are of dense finely fibrillated structure, containing no
cells. The tissue stains deeply in eosin and gradually fades off
into a less dense tissue containing a few cellular elements, ap-
parently stellate fibrous tissue cells, and finally into the ordi-
nary tissue of the ciliary body. The appearance is strikingly
that of osteoid tissue, though no osteoblasts were found. No
lens seen. The ciliary body has evidently been the seat of an
exudate which has organized and which extends across the eye
as a fibrous septum and is a direct continuation of an organized
exudate evidently taking place from the choroid. The outer
layer of the choroid is slightly detached from the sclera in
places. It shows well marked congestion and a diffuse round
celled infiltration, and is atrophied in places. In apposition with
the choroid and apparently involving the chorio capillaris is an
organized exudate which was spoken of before. This tissue
consists of a mesh-work of fibrillæ supporting fairly numerous
spindle and stellate connective tissue cells. Round cells are
also scattered diffusely throughout this tissue. Here and there
are areas, denser in character, of delicately fibrillated structure
supporting only a few cells of the stellate connective tissue
variety, which in favorable places are seen to grow gradually
denser and fade into well formed bone. The stellate connective
tissue cells with their branches very evidently become bone
corpuscles in lacunæ with their canilicula. Still other portions
of this section show areas of completely formed bone surround-
ing portions of loose connective tissue containing large blood
vessels. In others the blood vessels are surrounded by fat
tissue, as in Haversian canals. In very few places do we see
blood vessels coming in close contact with the new bone forma-
tion, but they are always surrounded by a loose connective or
fat tissue. No traces of the retina are seen.

ANALYSIS OF 42 CASES OF

TABULATION OF CASES OF

| Case | By Whom Reported | Year | Patient's Age | Sex | Reason for Removal of Eye | Etiology | Time Elapsing since Primary Lesion | Sympathetic Irritation |
|---|---|---|---|---|---|---|---|---|
| 1 | H. Berthold | 1870 | 45 | Male | O. S. Phthisis bulbi with pain. Diagnosis — Intraocular tumor | | | |
| 2 | E. Berthold | 1871 | 30 | Male | O. D. Severe pain. Blindness | Injury | 20 years | Yes |
| 3 | H. Knapp | 1871 | 17 | Female | Blind for three years. Phthisis bulbi. O. S. Repeated attacks of inflammation | Inflammation | Since childhood | Yes |
| 4 | H. Knapp | 1871 | 60 | Male | Phthisis bulbi. O. S. Repeated attacks of inflammation. Eye tender. Cornea opaque | Injury | 45 years | Yes |
| 5 | H. Knapp | 1871 | 45 | Male | Detached retina. Irido-cyclitis | Injury | 5 years | Yes |
| 6 | H. Knapp | 1871 | 38 | Male | Detached retina. Irido-cyclitis | Injury | ........... | Yes |
| 7 | H. Knapp | 1871 | .... | Female | O. S. Keratitis. Irido-cyclitis | Inflammation | 19 years | ......... |
| 8 | H. Schiess-Gemuseus | 1873 | 26 | Male | O. D. Inflammation. Severe pain. Clinical diagnosis — Tumor; secondary glaucoma; detached retina | ............. | ............. | ............. |
| 9 | H. Schiess-Gemuseus | 1873 | 35 | Male | O. D. Inflammation. Iridectomy five years before. Tumor. Phthisis bulbi | Inflammation | 6 years | ......... |
| 10 | H. Schiess-Gemuseus | 1873 | .... | Male | O. S. Blindness. With chronic iritis and chronic retinitis | Inflammation | Since childhood | ......... |
| 11 | H. Schiess-Gemuseus | 1873 | .... | ........ | Phthisis bulbi | Injury | 10 years | ......... |
| 12 | H. Schiess-Gemuseus | 1873 | .... | ........ | Phthisis bulbi. Irido-cyclitis. Plastic choroido-retinitis | ............. | ............. | ............. |
| 13 | H. Schiess-Gemuseus | 1873 | .... | ........ | Irido-cyclitis. Detached retina | ............. | ............. | ............. |
| 14 | H. Schiess-Gemuseus | 1873 | 16 | Female | O. S. Phthisis bulbi. Irido-cyclitis. Choroido-retinitis | Inflammation | 10 years | ......... |
| 15 | H. Schiess-Gemuseus | 1873 | .... | ........ | Phthisis bulbi. Detached retina | ............. | ............. | ............. |
| 16 | H. Wagner | 1873 | 48 | Male | O. S. Phthisis bulbi. Complete amaurosis | Injury | 35 years | Yes |
| 17 | M. Boncheron | 1875 | 26 | Male | Phthisis bulbi. Sympathetic inflammation twenty years later | Injury | 23 years | Yes |
| 18 | Dianoux | 1880 | 50 | Male | Phthisis bulbi. Detached retina | Inflammation | ............. | Yes |
| 19 | W. R. Amick | 1880 | 50 | Male | O. S. Malignant tumor of iris and choroid. Iridectomy done. Subsequent enucleation | Injury | 27 years | Yes |
| 20 | Wadsworth | 1880 | .... | Male | O. D. Recurring attacks of inflammation and tenderness | Injury | 14 years | Yes |
| 21 | W. Goldzieher | 1880 | 45 | Male | Blind. Choroiditis. Severe pain | Injury | ............. | ......... |
| 22 | W. Goldzieher | 1880 | .... | Female | O D. Phthisis bulbi. Eye painful. Irido-cyclitis | ............. | ............. | ......... |

# OSSIFICATION OF THE CHOROID.

## OSSIFIC GROWTHS IN THE EYE.

| Character of New Growth — Macroscopically. | Character of New Growth — Histologically. | Development of Bone. | Other Pathological Conditions. | Case. |
|---|---|---|---|---|
| Tumor, 1 c. m. in diameter. Hard masses on outside | Spindle-celled sarcoma and small masses of true bone, with characteristic bone corpuscles and lamellar systems | ................................ | ................................ | 1 |
| Complete shell | Normal bone tissue which contained marrow spaces filled with large fat cells | In connective tissue consisting of meshwork containing necrotic cells and leucocytes | Posterior synechia | 2 |
| Complete shell. Septum not ossified | True bone with concentric arrangement of bone corpuscles about nutrient canals | No cartilage or membrane. Soft layer of delicate connective tissue fibres and round cells — abundant — lying within the bone shell and contined across the eye shell posterior to the lens | Posterior synechia. Calcareous and fibroid lens. Slight fibrous change of outer layer of choroid. Retina degenerated | 3 |
| Septum ossified. Ring felt, 1½ m. m. broad | True bone in different stages of ossification readily made out | Different stages of ossification seen in tissues of the septum, composed of a fibrillous matrix filled with round, spindle, and stellate cells | Degenerated lens. Retina shows fibrous change. Cornea opaque | 4 |
| Partial shell; also small tumor in septum | True bone in both places | Osseous tumor lying in the soft granular-looking tissue enclosed by the coarcted retina | Degenerated and shrunken lens. Detached retina. Atrophied choroid. Fibroid degeneration of iris | 5 |
| Partial shell. Largely on one side | Thin shell of bone | Bone developed from the material exuded from the choroid | Detached retina with F. B. in fibrous tissue posterior to lens. Old choroiditis | 6 |
| Complete shell; also ossification of septum | True bone formation | Ossification of the inner layers of the choroid and of the fibrous septum, following an old irido-choroiditis | Detached retina. Ciliary bodies and iris thickened. Lens shrunken | 7 |
| Islands of bony tissue | Islands of bony tissue with bone corpuscles | Layer of new-formed tissue on choroid. Inflammatory hyperplasia. New-formed blood vessels. Round cell infiltration | Retina thin and atrophied | 8 |
| Tumor. Partial shell | Melanotic sarcoma. Partial bony shell | Small masses of bone lying in connective tissue | Degenerated lens | 9 |
| Partial shell | Plates of bone with bone corpuscles | ................................ | Fibrous lens | 10 |
| Partial shell | Bony tissue | Bone lying in connective tissue | Retina absent | 11 |
| Partial shell | Layer of new formed bone | ................................ | ................................ | 12 |
| Partial shell | Atrophied choroid covered with thin layer of bone | Bone lying in connective tissue | ................................ | 13 |
| Islands of bone | True bone formation with bone corpuscles | ................................ | ................................ | 14 |
| Partial shell | Masses of bone | Bone contained in connective tissue layer | ................................ | 15 |
| Small hard tumor projecting from choroid | True bone tissue | ................................ | ................................ | 16 |
| Plaque of bone | True bone formation | Bone lying in fibrous tissue | Detached retina. Vitreous body transformed into fibrous tissue | 17 |
| Complete shell | Perfectly formed bone with osteoplasts and bony canals and vascular channels | ................................ | Detached retina. Old inflammatory exudate | 18 |
| Partial shell | True bone | ................................ | Tumor, probably malignant. Detached retina | 19 |
| Partial shell | True bone formation | ................................ | Calcareous lens | 20 |
| Islands of bone | True bone involving the chorio-capillaris and retina. Both thickened and changed | Metaplasia of the organized exudates of the chorio-capillaries and retina with three stages of ossification | Vitreous liquefied. Retina fibrous in places, proliferating in others | 21 |
| Ossification of septum | Ossified septum with stellate bone corpuscles. Osteoid tissue extends into lens | Metaplasia of cyclitic membrane, with three stages of ossification | Detached retina and corpus ciliare. Obliterated anterior chamber. Iris adherent to cornea and lens | 22 |

TABULATION OF CASES OF OSSIFIC

| Case | By Whom Reported. | Year. | Patient's Age. | Sex. | Reason for Removal of Eye. | Etiology. | Time Elapsing since Primary Lesion. | Sympathetic Irritation. |
|---|---|---|---|---|---|---|---|---|
| 23 | W. Goldzieher | 1880 | .... | ........ | Atrophied bulb | ........ .... | ............. .... .. | |
| 24 | Dianoux | 1881 | .... | Female | Phthisis bulbi | ............. | ............. | Yes |
| 25 | Dianoux | 1881 | .... | ........ | Phthisis bulbi | ............. | ............. | Yes |
| 26 | Hoene | 1882 | .... | ....... | O. D. Iridectomy. Subsequent enucleation | Injury | ... ........... | ........ |
| 27 | Hoene | 1882 | .... | ........ | Eye enucleated — for sympathetic inflammation. Lens removed at previous operation | ............. | ............. | Yes |
| 28 | J. Fontan | 1883 | .... | ....... | Eye removed after death | ............. | ............. | Yes |
| 29 | J. Fontan | 1883 | .... | ....... | ............................ | ............. | ............. | ........ |
| 30 | J. Fontan | 1883 | .... | ........ | ......................... | ......... | ............. | ..... .... |
| 31 | C. J. Kipp | 1883 | 22 | Male | Irido-cyclitis. Had cataract since birth | No cause | ............. | ........ |
| 32 | T. H. Wood | 1890 | 25 | Female | O. S. Phthisis bulbi. Neuralgic pain. Blind. Following ophthalmia neonatorum | Inflammation | 25 years | Yes |
| 33 | T. H. Wood | 1891 | 27 | Female | O. S. Inflammation | Inflammation | 5 years | Yes |
| 34 | T. Reid | 1892 | 26 | Male | O. S. Gradual loss of sight. No pain | No apparent cause | 12 years | ........ |
| 35 | D. De Beck | 1897 | 59 | Male | O. S. Irido - cyclo - choroiditis. Phthisis bulbi | Injury | 21 years | Yes |
| 36 | Robert L. Randolph | 1900 | .... | Male | Eye removed after death | Injury | Since childhood | .. ..... |
| 37 | David Webster | 1901 | 18 | Male | O. D. Phthisis bulbi. Recurring attacks of inflammation | Injury | 15 years | Yes |
| 38 | David Webster | 1901 | 22 | Female | Enucleation for sympathetic inflammation. O. D. Blind, following original inflammation | Inflammation | 20 years | Yes |
| 39 | Millikin and Darby | 1902 | 25 | Male | Phthisis bulbi. Blind | Injury | 18 years | Yes |
| 40 | Millikin and Darby | 1902 | 17 | Female | Phthisis bulbi. Blind | Injury | 16 years | No |
| 41 | Millikin and Darby | 1902 | 39 | Female | Phthisis bulbi. Blind | Injury | 36 years | Yes |
| 42 | Millikin and Darby | 1902 | 47 | Male | O. S. Phthisis bulbi. Blind. Recurring attacks of inflammation | Injury | 3 years | No |

GROWTHS IN THE EYE.— CONTINUED.

| Character of New Growth — Macroscopically. | Character of New Growth — Histologically. | Development of Bone. | Other Pathological Conditions. | Case. |
|---|---|---|---|---|
| Bony shell occupying position of lens | True bone | Ossification of organized exudate, extending about lens from the cyclitic membrane or septum | ..... ..................... | 23 |
| Hard mass occupying about one-third interior of eye | True bone having osteoplasts in bony canals | ................................ | ............................ | 24 |
| Hard shell occupying region of choroid and ciliary processes | True bone | ................................ | ............................ | 25 |
| Complete shell and ossification of septum | Bony lamellæ, forming Haversian canals | Bone lies in connective tissue | Posterior synechia. Cellular infiltration of the sclera. Choroid shows fibroid thickening | 26 |
| Partial shell | True bone formation | Attached to the thickened and fibrous choroid | Choroid and iris atrophied. Optic nerve atrophied. Choroid shows fibrous thickening near and bony shell. Also thickening and round-celled infiltration of sclera | 27 |
| Partial shell | Compact plates of bone separated here and there by medullary spaces | ................................ | ............................ | 28 |
| Islands of bone | Islands of compact bone | Contained in the thick fibrous choroid, which had been the seat of a fibrinous exudation | ............. ............. | 29 |
| Small masses of bone | True bone | Masses of bone contained in the thickened and fibrous choroid | ....................... .......... | 30 |
| Complete shell. No ossification of septum | Normal bone | ................... ........... | Posterior synechia Calcareous lens. Detached retina. Choroid thickened. Aperture for optic nerve. Atrophic iris | 31 |
| Complete shell | True bone | ............................. | Atrophied optic nerve. Fibrous cornea. Outer layer of choroid degenerated. Retina and vitreous degenerated. Aperture for optic nerve. Lens absent | 32 |
| Partial shell | True bone | ............................. | Detached retina. Calcareous lens | 33 |
| Partial shell | True bone. Numerous lacunæ and canaliculi, in some parts concentrically arranged about rudimentary Haversian systems | Place of chorio-capillaris taken by an exudate containing spindle cells, in the midst of which the osseous capsule has developed | Detached retina. Calcareous lens | 34 |
| Complete shell | True bone | ............................. | Optic nerve atrophied. Detached retina. Lens atrophic. Aperture for optic nerve | 35 |
| Partial shell | True bone | ...................................... | ..............................√..... | 36 |
| Complete shell | True bone | .......... ....................... | ........... ................ | 37 |
| Partial shell | Resembles cancellous tissue of true bone with its concentric lamellæ and irregularly formed Haversian canals | Tissue about bone contains numerous leucocytes. No choroidal vessels, except in deeper parts, where there is choroidal pigment | Cornea thickened. Deep anterior chamber. Atrophic ciliary body. Calcareous lens. Detached retina | 38 |
| Hard mass in septum | True bone with bone corpuscles in lacunæ and Haversian canals | Metaplasia of fibrous tissue into bone | Detached retina. Calcareous lens | 39 |
| Complete shell with partial ossification of septum | Same | Same | Detached retina. Calcareous lens | 40 |
| Septum not ossified. Partial shell | Same | Same. Tissue similar to that of the septum surrounds lens | Detached retina. Calcareous lens | 41 |
| Bony masses | Same | Same. Osteoid-looking tissue at the base of several ciliary processes | Retina and lens absent | 42 |

ETIOLOGY.

*Age.* After childhood, age seems to have little or no influence in the development of bone in the eye. In 25 instances in which the age was given the ages ranged from 16 to 59 years.

*Sex.* Although twice as many males have been reported as females it seems highly probable that this factor is of little etiological importance.

*Previous Inflammation.* In 29 cases in which there were definite statements regarding this factor there was no inflammation in two eyes, but both had been blind for over ten years. In the other 27 cases 16 gave a history of injury a number of years previous to the enucleation. The other nine cases gave history of inflammation coming on insidiously in the eye several years before enucleation.

*The Time Elapsing since the Primary Lesion.* Data were given in 24 cases. No cases of ossification reported are in less than three years after primary inflammation of the eye. Four out of 24 cases reported under ten years. The eye affected was designated in 21 cases showing 8 right and 13 left eyes.

Phthisis bulbi was noted as being a prominent characteristic in 22 cases. Blindness noted in 11 cases. Pain in enucleated eye, 10. No pain reported in 2. Sympathetic irritation was recorded in 22 cases, and was usually one of the most potent reasons for enucleation. The absence of sympathetic irritation was recorded in 2 cases.

*Other Pathological Conditions.* The frequency with which certain other pathological conditions were found in these eyes containing bone deserves to be noted. In 21 out of the 42 cases the retina was reported as degenerated and usually detached. Atrophy and degeneration of the lens recorded in seventeen cases.

*Reasons for Enucleation.* As was stated above, 22 cases were reported as having had sympathetic irritation, and this was by far the most important indication for removal. In 8 other cases enucleation was practiced on account of recurring attacks of inflammation and pain. Two eyes were removed on account of

melanotic sarcoma of the choroid, and bone masses were found
on the periphery of the sarcoma. One eye was removed after
death. The cause for removal of 9 other eyes is not recorded.

*Position of Bone Mass.* · Recorded in 42 cases. By far the
greater number of cases (27) report specimens containing a par-
tial shell of bone or masses or islands of bone just internal to
the choroid. In 11 cases the shells of bone were said to com-
pletely cover the internal surface of the choroid.

The septum or ciliary membrane alone was reported as ossi-
fied in 3 cases. In 4 other instances the septum showed ossifica-
tion in connection with choroidal ossification. Ossification was
found in the exact region of the lens in one instance.

Besides these cases Pagenstecher has described bone at the
base of the retinal funnel. Berthold described bone at the pos-
terior surface of the iris. Shiess describes ossification in the
retina. Schiess-Gemuseus speaks of ossification in the con-
nective tissue common to both the retina and choroid. Gold-
zieher reports a case of ossification of the septum with the osteoid
tissue invading the posterior surface of the fibrous lens.

*Formation of Bone.* Twenty-five of the 42 cases reported de-
scribed the bone as lying in and developing from a loose fibrous
tissue which is evidently the result of an organized exudate in
the interior of the eye. No author as far as we can learn has
ever recorded the presence of cartilage in the eye.

Knapp in 1871, in discussing the formation of bone in the eye,
said that true ossification has never been demonstrated in the
crystalline lens, retina, cornea, iris, or vitreous body, but has
only been found in exudations from the choroid. The abrupt
termination of the osseous capsule at the ora serrata makes it
probable, in his opinion, that the chorio-capillaris are essential
in the production of osseous deposits, on account of its rich
blood supply. Subsequent inquiry strengthened his views.
Knapp further stated that the formation of bone in the eye is a
consequence and a final stage of a plastic inflammation of the
capillary layer of the choroid. He described the exudate as
investing the inner surface of the choroid and continuing in the

form of a transverse septum through the anterior part of the
vitreous humor behind the ciliary body and crystalline lens.
Knapp's descriptions are clear cut and accurate, and much of his
interpretation of the process might have been written at the
present time.   During the next few years several cases were re-
ported by such able men as Pagenstecher, Berthold, Schiess,
Schiess-Gemuseus, Alt, and Goldzieher on bone developing in
exudations other than those derived from the choroid.   These
cases prove conclusively that ossification may occur in the
fibrous tissue of organized exudates in the retina and uveal tracts,
or that such an exudate originating in the choroid and invading
other tissues such as the retina may ossify.   Now the essential
factor necessary for ossification is a new formed vascular con-
nective tissue.   These conditions are best met in organized
exudate from the uveal tract, the vascular tunic of the eye.   The
few cases reported as involving the retina can be explained by
the involvement of that organ in the original inflammation from
the neighboring choroid.   Or we might call it an ossification of
an organized choroidal exudate which had invaded the other
tissues.   The ossification about a lens may be explained in a
similar way.   The inflammatory exudate which forms a septum
by extending across the eye posterior to the lens, may in some
instances extend about the lens or even penetrate the lens sub-
stance and finally may become organized and then ossify.
Knapp considered this septum as a portion of the choroidal
exudate, but Goldzieher speaks of it as a " cyclitic membrane."
The fact remains that ossification occurs in organized exudates
from the internal structures of the eye and not in the stroma of
an inflamed structure.   No particles of bone have ever been
demonstrated in the stroma of the choroid, ciliary body, or iris.
Ossification has never been observed in the cornea, as the con-
ditions there are entirely unfavorable to bone formation.   That
the inflammatory exudate from the choroid is not the only tissue
in the eye capable of undergoing ossification was demonstrated
by Alt in 1871, when he discovered ossific processes as having
taken place in the colloid excrescences of the lamina vitrea

choroidiæ. Goldzieher in 1880 in discussing this subject stated
that according to Sattler the lamina vitrea is a kind of connective
tissue made up of wonderfully delicate fibrillæ having a lattice
work structure on its external surface toward the capillaries.
He believes that following an old inflammation a hyaline ma-
terial is usually deposited in this irregular, thickened, and or-
ganized lamina vitrea, the so-called " colloid excrescences " of
Alt. At times, however, after the organization has taken place
calcareous salts may be deposited here instead of the hyaline
material. Alt reports that he found " colloid excrescences " in
seven out of one hundred and fifty eyes examined, and that only
one or two of these seven showed definite bone formation and
three showed calcareous degeneration. Alt also reports having
examined fourteen cases of ossification of the choroid and found
that every one took place in the organized exudate from the
chorio-capillaris, as had been described by Knapp and Pagen-
stecher. The mode of development of bone in the eye has been
ably discussed by Goldzieher in 1880, whose views have been up-
held by Ware, 1886, Drake Brochman, 1889, and De Beck, 1897.
The process of ossification is one similar to that of early per-
iosteal bone formation. Cartilage has never been demonstrated
in this variety of bone formation. The meta-plasia of fibrous
tissue into bone has also been discussed extensively by Paul
Rohmer and Kurt Pollack in their articles on ossification occur-
ring in atheromatous heart valves, arteries, and in calcareous
nodules in the lung. The results obtained by these men were
very similar and coincide with the method of bone develop-
ment in the eye. They, however, always found their bony
plaques in fibrous tissue about some calcareous nodule. This
organized inflammatory exudate in an eye from which bone may
be developed is made up of loose fibrillæ with a reticulated struc-
ture supporting a moderate number of spindle and stellate con-
nective tissue cells and some small round cells. This tissue is
well supplied with blood vessels and usually contains small scat-
tered areas of choroidal pigment. In a suitable specimen where
the process of development is easily seen this tissue as it ap-
proaches the fully developed bone becomes denser. The loose

intercellular substance becomes replaced by numerous delicate interlacing fibrillæ, making a dense homogeneous matrix containing few cellular elements. The intercellular substance becomes more homogeneous and the cellular elements become fewer and more evenly distributed as the bone is approached. As yet no lacunæ or canaliculi are seen, but the processes of the stellate connective tissue cells can occasionally be recognized. Finally the deposition of lime salts take place, forming lacunæ, in which the connective tissue cells lie, which now represent the bone corpuscles. The lime salts are first deposited at a point farthest away from the larger blood vessels where the current in the capillaries is sluggish. Hence we sometimes see in these specimens areas of new formed bone in the vicinity of a small blood vessel, but there always exists a considerable space about this vessel in which ossification has not taken place. In the more recent specimens the vessels are seen surrounded by the ordinary loose connective tissue from which bone is primarily formed. In ossifications of long standing the ossified tissue approaches close to a vessel and ends abruptly. The vessel itself is surrounded by a loose reticulated structure containing numerous fat cells and a few epitheloid cells.

## CONCLUSIONS.

Ossification of the choroid is of moderately rare occurrence, though probably more common than is generally supposed. Careful search of the literature has revealed thirty-eight undoubted cases reported in the last thirty years. Age has little to do with ossification, as it occurs in all ages, though very rarely under fifteen years.

*Sex.* Ossification has been reported in the enucleated eye of about twice as many males as females, though this probably only indicates that traumatism destroying the eye is more common in males than females. Previous inflammation is probably the chief etiological factor in producing this condition. Between 60 and 75 per cent. of these cases are reported as due to inflammation, the result of injury.

Time elapsing since primary lesions has usually been from ten to thirty years. It has sometimes been found in eyes

enucleated less than ten years after primary lesions, but very rarely in less than five years. The relative frequency as to which eye was the more often injured shows nothing, as each eye had been enucleated about the same number of times.

Sympathetic irritation was the cause for removal of more than one-half of the cases reported.

Phthisis bulbi was noted as a prominent characteristic in about one-half the cases.

Blindness, though only recorded in one-third of the cases, was probably present in almost all, if not all, cases. Faint light perception was mentioned in one case. Pain in the enucleated eye was a prominent symptom in one-fourth of the cases reported. Detached or degenerated retina has been noted in over one-half the reported cases. An atrophic and degenerated lens was noted in about one-half of the cases.

Position of the bony mass. Two-thirds of the cases were those of partial shells or masses of bone springing from the choroid in the posterior part of the eyeball. A complete shell over the inner surface of the choroid was reported in about one-fourth of the cases, but some of these reports were very short and abbreviated, so probably the number is a little high. A few cases of ossification have been reported occurring in the fibrous septum posterior to the lens. Finally, a very few cases report an involvement of the retina and lens. Regarding the formation of bone we may say that ossification only takes place in an eye in which a long standing inflammation has occurred. Ossification almost always takes place in the organized exudate of the chorio-capillaris. This exudate at times involves other structures in the eye where ossification may subsequently occur. The essential for ossification is a vascular new-formed connective tissue, the result of an organized inflammatory exudate. Rarely ossification takes place in the lamina vitrea choroidæ, thickened and showing slight organization, the result of an old inflammation. The deposit of lime salts in osteoid tissue always occurs first at a point farthest away from the larger blood vessels.

### BIBLIOGRAPHY.

Berthold, H. Ein phthisischer Augapfel mit theils erweichtem, theils verknöchertem Chorioidealsarkom. Klin. Monatabl, f. Augenh. Erlang., 1870, VIII, 19-24.

Berthold, E. Verknöcherung der Chorioidea: Neubildung von Glashäuten: eigenthümliches Verhatten des Seheerven. Arch. f. Ophth., Berl., 1871, XVII, 1 Abth., 196-202.

Knapp, H. Formation of bone in the eye. Arch. of Ophth., N. Y., 1871, Vol. II, 1-35.

Schiess-Gemuseus, H. Beitrag zur Sehn. von der Knochen neubildung in der Chorioridea. Arch. of Ophth., Berl., 1873, XIX, 1 Abth., 202-220, 1 pt.

Wagner, H. Eine Hyperostose der Chorioidea ueben diffuser Verknöcherung derselber. 8° Halle, 1873.

Jeaffreson, C. S. Ossification of a large portion of the choroid following chronic traumatic inflammation. Lancet, Lond., 1873, II, 413.

Boncheron. Ossification de la Choroïde. Bull. soc. Anat. de Par., 1875, I, 108.

Laquer. Ein Fall von Ossification der Chorioidea mit ophthalmoscopischem Befunde. Arch. f. Augen. u. Ohrenh., Wiesb., 1877, VI, 29-35.

Dianoux. Ossification de la Choroïde. Bull. soc. Anat. de Nantes, 1879, Par., 1880, 66.

Amick, W. R. Ossification of the choroid: malignant tumor: enucleation and sympathetic ophthalmia. Cincin. m. New's., 1880, N. S., IX, 505-512.

Wadsworth. Osseous deposits in choroid. Extr. Rec. Bost. Soc. m. Improve., 1880, VII, 78.

Dianoux. Ossification de la Choroïde. Bull. soc. Anat. de Nantes, 1880, Par., 1881, IV, 95.

Goldzieher, W. Ossification in the eye. Arch. of Ophth. & Ot., N. Y., 1880, IX, 300-317.

Hoene, J. Recherches microscopiques sur les ossifications choroïdiennes. Rec. d'Ophth., Par., 1882, 3 s., IV, 708-718.

Fontan, J. Ossification de la Choroïde: examen. de trois

bulbes ocularies atteints de cette ossification.  Rec. d'Ophth., Par., 1883, 3 s., V, 205-211, 2 pt.

Frost, W. A.  Ossification of choroid, causing repeated attacks of sympathetic irritation.  Tr. Ophth. Soc. U. Kingdom, Lond., 1883-4, IV, 171.

Kipp, C. J.  Ossification of the choroid.  Tr. Am. Ophth. Soc., 1883, III, Part 4, 564.

Ware, L.  Ossification of the choroid.  J. Amer. M. Asso., Chicago, 1886, VI, 39.

Laënnec.  Ossification de la choroïde.  Bull. Soc. Anat. de Nantes, 1880, Par., 1890, XII, 17.

Ruiz, P.  Ossification totale de la choroïde: glaucome sympathique dans un oeil primitivement opéré de cataracte: rupture spontanée de la cicatrice: énucléation de l'oeil sympathizant: guérison.  Rec. d'Ophth., Par., 1889, 3 s.. XI, 29-32.

Drake-Brockman, E. T.  Case of ossification of the choroid. Brit. Med. J., Lond., 1889, I, 585.

Ehrhardt.  Ossification de la choroïde, et décellement " en paraphine " de la rétine ayant provoqué une ophthalmis sympathique.  Bull. Soc. Anat. de Par.. 1890, LXV, 25.

Wood, T. H.  Ossification of choroid.  Arch. Ophth., N. Y., 1890, XIX, 388.  Ophth. Rec., Nashville, 1891, I, 24.

Reid, T.  Ossification of the choroid.  Tr. Glasg. Path. & Clin. Soc. (1886-91), 1892, III, 96.

Meighan, T. S.  A case of ossification of the choroid.  Tr. Glasg. Path. & Clin. Soc., 1886, 1891, 1892, III, 120.

Romano-Catania.  Ossification of the Choroid.  Arch. di Ottalm., 1895, II, 11 p., 345.

De Beck, D.  Ossification of the choroid.  Tr. of Acad. of M., Cincin., 1897, 269, 272.

Randolph, R. L.  Ossification of the choroid.  Ophthal. Section A. M. A., 1900, 203-206.

Webster, D.  Two cases of ossification of the choroid.  Arch. of Ophth., 1901, XXX, pp. 23-26.

Kurt Pollack.  Ueber Knochenbildungen in der Lunge.

Virchow's Archives Fur Pathologische Anatomie und Physi-
ologie, und fur klinische Medicin.   Band 165 Juli Seite, 120-189.

Paul Rohmer.   Ueber Knochenbildung in verkalkten en-
docarditischen Heerden.   Reference same as above.   Band 166,
October, Seite 13-40.

# The Frequency, Site and Course of Tuberculosis in Cleveland

As Shown by 658 Autopsy Records from Lakeside Hospital and the Pathologic Laboratory of the Western Reserve University

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It is the object of our paper to deduce some statistics of value regarding the prevalence of tuberculosis in Cleveland as shown in the record of 658 autopsies. These records have been derived from two sources: first, those from the Pathologic Laboratory of the Medical College of Western Reserve University during the last eight years; and those from the Pathologic Laboratory of The Lakeside Hospital since its foundation four years ago. The records from the Medical College consist of 320 autopsies derived from various sources. About two-thirds of these were from autopsies performed at the City Hospital, the remainder from autopsies done at Charity and St. Alexis Hospitals and in private residences. The Lakeside Hospital records comprise 338 autopsies, practically all of which were performed at that institution. Of these 658 autopsies 195 or 29.6% showed definite tuberculosis. This includes all cases which showed the presence of the tubercle histologically or macroscopically; cases having caseous or calcified bronchial lymph glands, and cases showing very evident fibroid change at an apex of a lung with apical adhesions or puckering.

Active tuberculous processes were found in 120 cases, which is 18% of the 658 autopsies analyzed, or 61.5% of the cases showing definite tuberculous lesions. We include among our cases of active tuberculosis those showing the tubercle histologically, and all cases having caseous bronchial glands with an evident focus in some other part of the body. The nonactive cases comprise those having caseous or calcified bronchial glands without demonstrable tuberculous lesions elsewhere, and also those cases in which there is an evident fibroid change at an apex of a lung with apical adhesions or puckering. Of the 658 cases analyzed tuberculosis was

the cause of death in 72, 11% of all cases, or 60% of those having active tuberculosis.

Of the 463 cases not considered tuberculous 38 or 5¾% of the total number showed localized fibrous adhesions at an apex of a lung or else well-marked apical puckering. There were found 139 other cases where fibrous adhesions had been noted in various places over the surface of the lungs. A large percent of these 139 cases either had well-marked arteriosclerosis, or a history of pneumonia, pleurisy or rheumatism. Of these cases we feel that the first group, 5¾% of all cases, should be included with our cases of definite tuberculosis. We are confident that this group as well as a portion of the second group would prove definitely tuberculous if examined exhaustively for tuberculous lesions.

In the cases of *active* tuberculosis in which the age is noted we find under 10, 4.6%; from 10 to 20, 4.6%; from 20 to 30, 19.8%; from 30 to 40, 22.6%; from 40 to 50, 17.9%; from 50 to 60, 15%; over 60, 15%.

The mortality per decade of those cases showing active tuberculosis is as follows: Under 10, 80%; from 10 to 20, 80%; from 20 to 30, 56%; from 30 to 40, 50%; from 40 to 50, 42%; from 50 to 60, 50%; over 60, 12.5%.

The distribution of tuberculosis throughout the body was as follows: Lungs, 167 cases, 85.5%; bronchial glands, 63 cases, 37.4%; spleen, 23 cases, 11.8%; intestines, 21 cases, 10.7%; kidney, 19 cases, 9.7%; liver, 15 cases, 7.5%.

The nervous system was affected in 8 cases, the peritoneum in 7, the bones and joints in 7, the pericardium in 4, the adrenals in 4, the mesenteric glands in 3, the larynx in 2, the myocardium in 2, the voluntary muscles in 2, the fallopian tubes in 2, the pancreas in 2, the thyroid glands in 2, the cervical glands in 2, the prostate and thymus in 1 case each. The skin was not affected. Miliary and general tuberculosis was present in 28 cases or 14.3% of the definitely tuberculous cases.

The primary focus, as far as could be obtained from the autopsy records, was as follows: Lungs, 159 cases, 81.5%; bronchial glands, 30 cases, 15.4%; vertebrae, 3 cases; mesenteric and cervical glands, 2 cases each; peritoneum, 1 case.

In a recent article by Naegeli of Zurich, of 164 autopsies, 40% showed definite tuberculous change. In a later 344 autopsies the organs were examined very exhaustively with especial reference to the presence of tuberculous foci. Of these 97% showed tuberculosis.

It is only fair to suppose that our percentage of tuberculous lesions, 29.6%, is considerably less than is really the case, for the histologic examination did not have for its sole aim the diagnosis of tuberculosis. Also a number of autopsies were performed at private houses in which the lack of time and proper facilities made an exhaustive search impossible; moreover, tuberculosis is doubtless less frequent here than in Europe.

The autopsy records of Lakeside Hospital in comparison with those of the Medical School show about 10% more of definite tuberculous lesions, although cases of frank pulmonary tuberculosis are very rarely admitted to that Hospital. This difference is due to the fact that at Lakeside Hospital the organs are examined with especial care for tuberculous foci.

<div align="center">CONCLUSION</div>

1.   We wish to impress the fact that our figures of 29.6% of definite tuberculosis at autopsy fall considerably below the true figure, and so wish to include our 5¾% of cases with apical adhesions or puckering. Granting this, a total of 35.3% or 1/3 of all autopsies show tuberculous change, and this is a very conservative estimate.

2.   Active tuberculous processes were found in practically half of all cases showing definite tuberculosis.

3.   In over half of these active cases tuberculosis was the cause of death.

4.   Under 20 years of age active tuberculosis is almost always fatal. After this age the mortality of active tuberculosis steadily decreases, so that death from tuberculosis is comparatively rare in persons over 60 years of age.

5.   The relative frequency of tuberculosis in a few of the principal organs is in the order named, lungs, bronchial glands, spleen, intestines, kidney, liver and nervous system. The other portions of the body are comparatively rarely affected.

6.   The primary focus seemed almost invariably the lungs and occasionally the bronchial glands.

We wish to extend our thanks to Dr W. T. Howard, Jr., for his kindly assistance and supervision in compiling these statistics. To Dr Howard Ditrick we are also indebted for much assistance in the analysis of the autopsy records.

# A Bacteriologic Study of the Blank Cartridge.

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# A BACTERIOLOGIC STUDY OF THE BLANK CARTRIDGE.*

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It appears from statistics in THE JOURNAL of the American Medical Association, August 29, 1903, that of 392 cases of tetanus incident to accidents on the previous July 4, 363 followed wounds from the blank cartridge and the toy pistol. In other words, 92 per cent. of the tetanus cases were apparently attributable to wounds from blank cartridges.

Dr. A. I. Ludlow, assistant resident surgeon at the Lakeside Hospital, succeeded in isolating *B. tetani* from the blank cartridge wounds in one out of five fatal cases of tetanus, but cultivated the *B. aerogenes capsulatus* in four. In none of these cases was there emphysema nor emphysematous gangrene of the wounds, which were routinely treated by free incision and packing with iodoform gauze. In one of these which came to autopsy I failed to isolate *B. tetani* from the wound of the hand, but obtained *B. aerogenes capsulatus* from the local lesion and heart's blood. There was no gaseous emphysema of any organ.

These findings led me to investigate several makes of blank cartridges, and the results of these investigations form the basis of the present paper. The infectious agents concerned in these wounds (apart from the contents of the cartridge), mav come from the skin and parts of clothing introduced. These latter sources of infection were not considered.

### SOURCE OF MATERIAL.

The cartridges used were manufactured by the Peters Cartridge Co., the Winchester Arms Co., and the Union

Metallic Cartridge Co., and were bought in the open market at various times and places.

<div align="center">CULTURAL EXPERIMENTS.</div>

(A) *Wads.*—In both the cultural and animal experiments the wads were extracted with a sterile instrument, every care being taken to exclude accidental contamination.

The wads were placed in a 1 per cent. glucose bouillon, and incubated under anaërobic conditions (usually in Novy jars) at body temperature, for from 3 to 5 days, when coverslip preparations were studied. Not infrequently slender bacilli with end spores suggestive of *B. tetani* were seen. Nine cultures containing these tetanus-like bacilli were inoculated in fresh hematoma in the thigh of guinea-pigs. All of these animals survived but one, which died at the end of a month without symptoms of tetanus. These tetanus-like bacilli decolorized by Gram and were proved by cultural methods to be identical with a pseudo-tetanus bacillus discovered by Bain in blank cartridges. Many cultures contained a stout bacillus with square ends, apparently encapsulated, and subcultures made on glucose agar showed abundant gas formation. Nine rabbits injected with these gas-forming cultures, and killed ten minutes afterward, showed after from 8 to 20 hours' incubation marked gaseous emphysema, and *B. aerogenes capsulatus* was isolated from them all in pure culture. All efforts to demonstrate the presence of *B. tetani* failed. In a total of 250 wads examined by culture, the *B. aerogenes capsulatus* was demonstrated in sixty-six, or 26.4 per cent., and from sixty-one it was isolated in pure culture. Two of these were worked through all media, but in general the cultural characteristics on glucose agar, milk, and blood serum, together with the morphology, the capsule formation, the positive Gram stain, and the failure to grow aërobically, were deemed sufficient for identification. It is interesting to note that spore formation occurred in old milk and agar cultures, as well as on blood-serum. Some difficulty was experienced in separating *B. aerogenes capsulatus* from the other anaërobic organisms present in wads until Kitasato's method of heating for one hour at 80 degrees C. was adopted. It invariably survived this. That the explosion of cartridges neither kills nor inhibits the growth of *B. aero-*

*genes capsulatus* was demonstrated by shooting the wads into jars containing melted glucose agar, which on incubation gave abundant growth of this organism in four out of five experiments.

The following table gives the proportion in which *B. aerogenes capsulatus* was found in wads of the different makes:

| | Wads examined. | B. A. C. | Per cent. |
|---|---|---|---|
| Peters .32 caliber | 54 | 32 | 50.9 |
| Peters .22 caliber | 50 | 21 | .... |
| U. M. C. .32 caliber | 49 | 7 | 7.0 |
| U. M. C. .22 caliber | 50 | 0 | .... |
| Winchester .22 caliber | 47 | 6 | 12.7 |
| | 250 | | |

*(B) Powder.*—Cultures from the powder of 101 cartridges were usually sterile. Neither *B. tetani* nor *B. aerogenes capsulatus* was isolated.

### INOCULATION OF ANIMALS.

At the suggestion of Prof. William H. Welch, the rat was used as being probably the animal most susceptible to tetanus.

To give *B. tetani*, if present, the most favorable environment possible, use was made of two procedures, the second one of which has not been employed in similar investigations. The first is inoculation of fresh hematoma, which increases greatly the chances of growth of *B. tetani*. As to the second one, Vaillard and Rouget established that "tetanus spores when free from toxin are innocuous when not accompanied by another bacterium, unless protected from phagocytes." Twelve white rats were inoculated under strict aseptic precautions with wads from the Peters Co. 32 caliber cartridges. In addition, a loop of a pure aërobic culture was added, in six an attenuated *Staphylococcus pyogenes aureus* and in the remaining six *B. coli communis.* The skin was then closed by a stitch and covered with celloidin.

Nine of these rats died in convulsions, the tenth quietly, while the other two survived. The incubation period varied from sixty to seventy hours. The character of the convulsions differed from that usually described for animals. The first symptom was a marked spastic condition of the inoculated leg, which was held in extreme flexion, explainable by the laceration of the extensor muscles. Gradually this spastic state extended to the whole body, so that the animal would re-

tain its distorted shape in any position. In all, there was emprosthotonos, in two associated with pleurothotonos. The forelegs were held closely against the abdomen and the non-inoculated leg in extension. At short, irregular intervals there were definite convulsions, the most typical of which started with several rapid nods of the head, followed in order by clonic spasms of forelegs and hindlegs, passing in a few seconds into a tonic spasm of the whole body. In several, clonic spasms alone appeared. The convulsions lasted from one and a half to three hours, the animals all dying at the end of a spasm. At autopsy no lesions of internal organs were found. Smears from the meninges were negative for leucocytes and bacteria. Bearing in mind previous failures to cultivate *B. tetani* from wounds, it was thought wiser to subinoculate from these animals. Accordingly, the wads, with some necrotic tissue, were removed from six of the rats and inoculated into three guinea-pigs and three rabbits. The guinea-pigs died during the night, but the rabbits developed tetanus in about thirty hours. The character of the convulsions corresponded to the description in text-books.

In smears from the rats and guinea-pigs, a few spore-bearing bacilli morphologically resembling *B. tetani* appeared. These were somewhat more numerous from the rabbits. From one rat, only one such bacillus was seen after an hour's search. In all smears bacilli morphologically identical with *B. aerogenes capsulatus* were recognizable, together with numerous other organisms. Cultures were made from the wounds and wads on glucose bouillon and glucose agar, as well as blood serum. There was marked gas production, but repeated search failed to disclose *B. tetani*. Numerous subcultures, made both with and without Kitasato's method, were likewise negative. *B. aerogenes capsulatus* grew so rapidly and vigorously that it apparently crowded out *B. tetani*. Many anaërobic plates were also unsuccessful as regards *B. tetani*. In explanation of these failures, it may be said that the tetanus-like bacilli were extremely scanty, while *B. aerogenes capsulatus* was relatively abundant; and, further, that several other bacilli were present in the Peters wad, which resisted heating as well, one of these forming colonies much resembling those of *B. tetani*.

However, of five rabbits inoculated with five or six loops of the original cultures, three died in convulsions. Smears and cultures from their wounds were also entirely negative for *B. tetani,* though made as soon as symptoms of tetanus appeared.

The experiment was next tried of adding several crystals of urea to the material inoculated for its antichemotactic effect. In this rabbit the exudate was poor in leucocytes, and tetanus-like bacilli more numerous than in previous experiments, but *B. aerogenes capsulatus* had also increased proportionately and several series of plates were again negative for *B. tetani·*

A second series of inoculations with the Peters wads was next made. Three rats and three guinea-pigs were each inoculated with two wads, together with *Staphylococcus pyogenes mucus,* and several small crystals of urea. One rat and two pigs developed tetanus. As in the previous experiment, tetanus-like bacilli appeared in greater numbers than in the first series, but have not yet been isolated.

Inoculation experiments were also tried with the other brands of cartridges. In the case of the Union Metallic cartridges, the wads from the seven original bouillon cultures which yielded *B. aerogenes capsulatus* were used. One rat died without tetanic symptoms, the others survived. Likewise, thirteen wads of the Winchester cartridges, distributed among three rats and three guinea-pigs, produced no symptoms, and the animals survived the local suppuration produced by the staphylococcus.

Previous work has been done on this subject by Le Garde, Taylor, Wells, and the Boston Health Department, a total of 759 cartridges having been examined, both by cultures and animal inoculations, all with negative results for *B. tetani.* The only report of the finding of *B. tetani* in cartridges is made by R. N. Connolly, bacteriologist to the board of health of Newark, N. J. He bases his diagnosis, apparently, on the morphology and odor of cultures, and no inoculation of animals is reported. With regard to *B. aerogenes capsulatus,* Wells alone describes an obligate anaërobe which corresponds closely to this organism, but says it seemed to have motility, and it is not identified.

My thanks are due to Dr. W. T. Howard, Jr., and to Dr. Roger G. Perkins, for their valuable suggestions.

### CONCLUSIONS.

1. *B. aerogenes capsulatus* (Welch) was present in a large proportion of the wads of the three makes of cartridges examined.

2. The wads of the Peters Company, inoculated in rats, guinea-pigs and rabbits, produced characteristic symptoms of tetanus.

3. The powder of the three varieties of cartridges examined was negative for *B. tetani* and *B. aerogenes capsulatus*.

4. My efforts at isolation of *B. tetani* from the wads have so far been unsuccessful.

5. There is abundant evidence, from clinical observations and animal experiments, that the wads of certain blank cartridges contain *B. tetani*. Dr. Welch told me that he considered it diagnostic to see an animal in convulsions.

# A CASE OF TUBERCULOUS SALPINGITIS FROM WHICH THE TUBERCLE BACILLUS WAS GROWN.[1]

### BY

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Tuberculosis of the fallopian tubes is not infrequent, but cases in which it is possible to cultivate the specific bacillus from a tuberculous fallopian tube are among the exceptions. In fact, we have not been able to find a recorded instance in which this has been done. The history of a case follows :

CASE.—M. H., white, aged 21 years, was admitted to the gynecologic ward of Lakeside Hospital March 22, 1901. The family and personal history have no special bearing upon the case. She was married in June, 1900, and in December had a miscarriage at the third month of pregnancy. Catamenia commenced at the age of 14. They were regular for the first 10 months, but after this they appeared every two weeks, and sometimes more frequently. Prior to admission she had had a continuous flow for four weeks. She complained of the following symptoms : Dull pain in the lower abdomen extending down into the thighs, backache, a leukorrheal discharge, and constipation. On examination of the chest we were able to make out a few moist rales over both apices ; the heart was normal. The leukocyte count was 10,000. The urine showed a slight trace of albumin with a few hyaline casts. The temperature ranged from 98° to 99.2° F. On examination of the pelvic organs, made under general anesthesia, the following notes were recorded : " The vaginal outlet is slightly relaxed. The cervix crosses the axis of the vagina. The uterus is in normal position. The right tube and ovary are somewhat enlarged and adherent. The left tube and ovary are small, irregular in outline, and adherent."

*Operation.*—On March 28, 1901, curetting and abdominal section were performed by Dr. Robb. A small amount of endometrial debris was removed. The tubes and ovaries on both sides were adherent to each other and to the broad ligament. The vermiform appendix and the lower portion of the omentum were also bound down by adhesions. Both tubes and ovaries, and the vermiform appendix were removed, with a portion of the omentum. On inspection of the peritoneal surface of the tubes gray tubercles were visible, but on no other part of the abdominal peritoneum could any be detected. The abdomen was flushed out with saline solution, and sponged dry ; 500 cc.

[1] Read before the Cleveland Medical Society, March 14, 1902

were left in it and the wound was closed without drainage. The patient made an uninterrupted recovery, except for a slight hacking cough.

The sputum was examined and tubercle bacilli were found in small numbers. The temperature during the last 13 days of her stay at the hospital was never above 99° F. She was discharged April 29, 1901, much improved. Seven months after the operation she returned to the dispensary service of the hospital, complaining of a cough with occasional night sweats. With this exception, however, there was a marked improvement in her condition.

The pathologic and bacteriologic examination have the following results : [1]

*Pathologic Examination.*—On both macroscopic and microscopic examination the ovaries appeared normal, except for a few fibrous adhesions. The appendix was 8 cm. long, 5 mm. thick, and normal in appearance. The omentum was also normal. The uterine curettings showed no tuberculosis, though there was some chronic interstitial endometritis.

The right fallopian tube measured 20 cm. in length, and was very much convoluted, resembling a trumpet in shape. As regards width, it tapered from 3.25 cm. at the fimbriated extremity to 1 cm. at the isthmus. In color it was flesh pink, except at the more dilated portion, where it was tinged with yellow. The fimbriated extremity was occluded. The most striking feature, however, was the presence of small, gray, translucent tubercles scattered over the peritoneal surface. These were seen in larger numbers on the outer extremity of the tube, especially on the posterior surface. The wall seemed slightly thickened at the isthmus, but throughout the ampulla and the fimbria it was dilated, and fluctuation was readily detected. On puncturing this portion a thick, yellow, creamy pus exuded.

The left tube, though somewhat smaller in size, showed a condition similar to that of the right side. It measured 6 cm. in length and 1.5 cm. in width. It was very much distorted and bent upon itself. The fimbria was occluded. In the outer two-thirds fluctuation was elicited. A few miliary tubercles were seen on the distal half of the peritoneal surface. Pus of the same nature as that of the right side was found in the lumen of the tube.

On microscopic examination, the right fallopian tube presented a typical tuberculous salpingitis. The flat epithelium of the peritoneum was intact at the site of the adhesions. The underlying connective tissue was very vascular, and showed slight infiltration with lymphocytes, polymorphonuclear neutrophiles and eosinophiles. When sections were taken through a gray tubercle, characteristic areas showing a central giant-cell, surrounded by epithelioid and round-cells were observed. As a rule, there were three or four of these tubercles in each nodule. Between the fibers of the muscularis, there was an extensive infiltration of plasma cells, polymorphonuclear eosinophiles, polymorphonuclear neutrophiles, lymphocytes and mast cells. In some places the infiltrated muscle was hyaline, while at other points it had been replaced by fibrous connective tissue. Through the isthmus the muscular layer was very much hypertrophied. The lumen of the tube was

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[1] From the Pathologic Laboratory of the Lakeside Hospital.

filled with caseous material, compressing the underlying mucosa and submucosa. These two layers were the seat of diffuse tuberculosis, containing larger and smaller numbers of giant-cells. In sections taken through the internal extremity of the tube, it was observed that its lumen was free from exudate, the epithelium was intact, and the tubercles were found only in the muscularis.

The left fallopian tube presented a similar picture microscopically. The serous layer was the seat of a chronic perisalpingitis, and the muscular tissue was infiltrated to the same degree with round-cells. Toward the fimbria, the submucosa and mucosa were involved in the tuberculous process, and in some instances the tubercles had ruptured into the lumen. This latter contained a large amount of granular debris, among which appeared numerous nuclear fragments and a few polymorphonuclear neutrophiles. At the isthmus the lumen was intact and the epithelium appeared normal.

*Bacteriology.*—Coverslip preparations of the pus stained for tubercle bacilli proved negative. Cultures were made from each tube on glycerin agar and glucose bouillon potato, especial care being taken to obtain the loop from the tuberculous tissue rather than from the caseous material. The glucose bouillon potato was prepared by sterilizing potato in an excess of glucose bouillon. The culture tubes were sealed with paraffin and placed in the thermostat at 37° C. The glycerin-agar tubes showed no growth and remained sterile. Twenty-six days after inoculation a thin, glistening, greyish-white growth was detected on the potato. Coverslip preparations were stained by Gabbett's method and large clumps of acid-proof bacilli, morphologically identical with tubercle bacilli, were found in each potato culture. An emulsion was made by macerating the superficial growth in sterile glucose bouillon, and this was injected into the peritoneal cavity of a guineapig. Less than four months later the pig died and on examination an undermined ulcer was found on the abdominal wall with abscesses in the liver, spleen, lungs and the axillary and inguinal glands. Cultures were taken from all these tissues, as well as from the ulcerated area, the peritoneum, pericardium and right auricle, and all showed pure cultures of *B. pyocyaneus.* Coverslips were also made and stained with carbol-fuchsin and methylene blue, but the only one in which tubercle bacilli were demonstrated was the preparation from the lung, and here they were present only in small numbers. The organs were examined microscopically and only in the lungs was there any suggestion of tuberculosis. Here there was consolidation with cavity formation, but no characteristic tubercles were seen. However, on staining the tissue for tubercle bacilli they were found in large numbers. The animal had evidently been injured and become infected with *B. pyocyaneus* and died from pyemia with the formation of metastatic abscesses.

Several methods recommended for the detection of tubercle bacilli in tissues were employed, the one that yielded the best results being the following:

1. Stain slightly with alum-hematoxylin.
2. Wash in water.
3. Steam with carbol-fuchsin for three minutes.
4. Wash in water.
5. Decolorize with acid alcohol.
6. Very dilute ammonia.
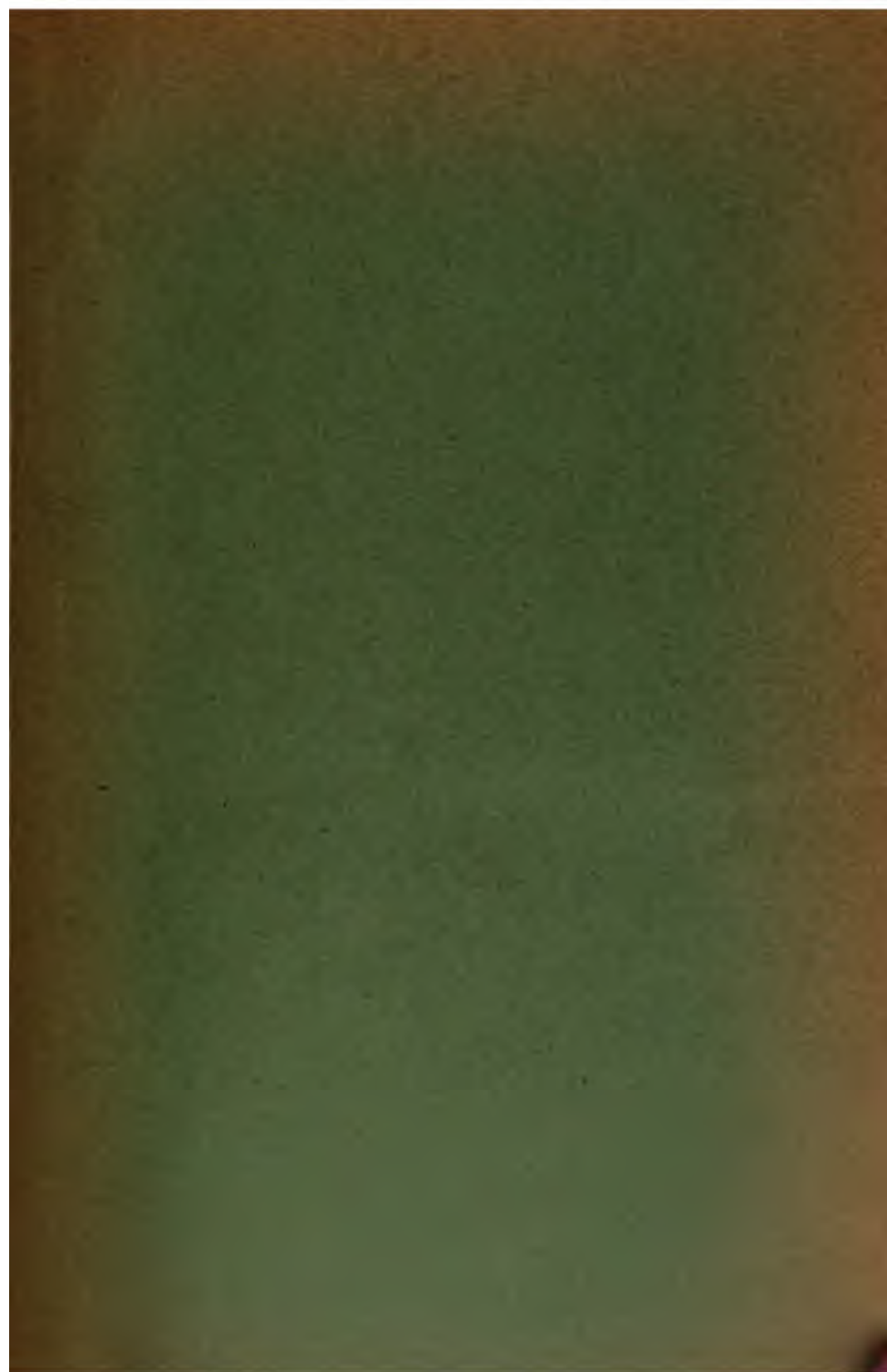7. Ninety-five per cent. alcohol till no fuchsin is left.

8. Clear in anilin oil and xylol.
9. Mount in Canada balsam.

On staining sections of the fallopian tubes as outlined above, the acid-proof bacilli were found in small numbers. As a rule they lay between the nuclei around the wall of the giant-cells, but some were found in the epithelioid zone. None was seen in the caseous material in the lumen.

In this case, then, we were able to demonstrate the presence of tubercle bacilli in the tissue of the fallopian tube, and to cultivate the organism found in this tissue, and then reproduce the same disease in the guineapig which had been inoculated with the bacilli from the primary lesion.
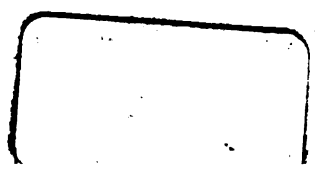
I wish to express my thanks to Professor William T. Howard, Jr., for his kind supervision of this work.